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     (FILE 'HOME' ENTERED AT 10:16:41 ON 23 JUN 2005)

     FILE 'STNGUIDE' ENTERED AT 10:16:54 ON 23 JUN 2005

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 10:17:40 ON 23 JUN 2005
L1         22912 S SPHINGOSINE
L2          1950 S L1 (W)KINASE?
L3           104 S HUMAN (W)L2
L4            54 DUP REM L3 (50 DUPLICATES REMOVED)
L5       7132348 S CLON? OR EXPRESS? OR RECOMBINANT
L6            36 S L4 AND L5
L7       3507345 S MIMETIC? OR DERIVATIVE? OR ANALOGUE?
L8           388 S L2 AND L7
L9          6947 S SPHINGOSINE-1-PHOSPHATE
L10          320 S L8 AND L9
L11          320 S L10 AND KINASE?
L12          211 DUP REM L11 (109 DUPLICATES REMOVED)
L13          126 S HUMAN AND L12
                 E PITSON S M/AU
L14          170 S E3-E7
                 E WATTENBERG B W/AU
L15          174 S E3-E9
                 E DIANDREA R J/AU
                 E GAMBLE J R/AU
L16          355 S E3
                 E VADAS M A/AU
L17         1272 S E3-E8
L18         1564 S L14 OR L15 OR L16 OR L17
L19          109 S L2 AND L18
L20           33 DUP REM L19 (76 DUPLICATES REMOVED)
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NEWS	16	APR 28	Improved searching of U.S. Patent Classifications for U.S. patent records in CA/CAplus
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NEWS	18	MAY 23	REGISTRY has been enhanced with source information from CHEMCATS
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=> s sphingosine
L1       22912 SPHINGOSINE

=> s l1 (w)kinase?
L2        1950 L1 (W) KINASE?

=> s human (w)l2
L3         104 HUMAN (W) L2
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=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 54 DUP REM L3 (50 DUPLICATES REMOVED)

=> d 1-54 ibib ab

L4 ANSWER 1 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:203242 HCAPLUS
DOCUMENT NUMBER: 142:296555
TITLE: Sphingosine Kinase 1 (SK1) Is Recruited to Nascent Phagosomes in Human Macrophages: Inhibition of SK1 Translocation by Mycobacterium tuberculosis
AUTHOR(S): Thompson, Christopher R.; Iyer, Shankar S.; Melrose, Natalie; VanOosten, Rebecca; Johnson, Korey; Pitson, Stuart M.; Obeid, Lina M.; Kusner, David J.
CORPORATE SOURCE: Inflammation Program, Departments of Internal Medicine, University of Iowa Carver College of Medicine, Coralville, IA, 52241, USA
SOURCE: Journal of Immunology (2005), 174(6), 3551-3561
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB M. tuberculosis (M.tb) is a leading cause of global infectious mortality. The pathogenesis of tuberculosis involves inhibition of phagosome maturation, leading to survival of M.tb within human macrophages. A key determinant is M.tb-induced inhibition of macrophage sphingosine kinase (SK) activity, which normally induces Ca2+ signaling and phagosome maturation. The authors' objective was to determine the spatial localization of SK during phagocytosis and its inhibition by M.tb. Stimulation of SK activity by killed M.tb, live Staphylococcus aureus, or latex beads was associated with translocation of cytosolic SK1 to the phagosome membrane. In contrast, SK1 did not associate with phagosomes containing live M.tb. To characterize the mechanism of phagosomal translocation, live cell confocal microscopy was used to compare the localization of wild-type SK1, catalytically inactive SK1G82D, and a phosphorylation-defective mutant that does not undergo plasma membrane translocation (SK1S225A). The magnitude and kinetics of translocation of SK1G82D and SK1S225A to latex bead phagosomes were indistinguishable from those of wild-type SK1, indicating that novel determinants regulate the association of SK1 with nascent phagosomes. These data are consistent with a model in which M.tb inhibits both the activation and phagosomal translocation of SK1 to block the localized Ca2+ transients required for phagosome maturation.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:330589 HCAPLUS
TITLE: Sphingosine kinase-1 enhances endothelial cell survival through a PECAM-1-dependent activation of PI-3K/Akt and regulation of Bcl-2 family members
AUTHOR(S): Limaye, Vidya; Li, Xiaochun; Hahn, Chris; Xia, Pu; Berndt, Michael C.; Vadas, Mathew A.; Gamble, Jennifer R.
CORPORATE SOURCE: Hanson Institute, Institute of Medical and Veterinary Science, Adelaide, Australia
SOURCE: Blood (2005), 105(8), 3169-3177
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Sphingosine-1-phosphate (S1P), the bioactive product of sphingosine kinase (SK) activation, is a survival factor for endothelial cells. The mechanism of SK-mediated survival was investigated in endothelial cells with moderately raised intracellular SK activity. Overexpression of SK mediated survival primarily through the activation of the phosphatidyl inositol 3-kinase (PI-3K)/protein kinase B (Akt/PKB) pathway and an associated up-regulation of the antiapoptotic protein B cell lymphoma gene 2 (Bcl-2) and down-regulation of the proapoptotic protein bisindolylmaleimide (Bcl-2 interacting mediator of cell death; Bim). In addition there was an up-regulation and dephosphorylation of the junctional mol. platelet endothelial cell adhesion mol.-1 (PECAM-1), which was obligatory for activation of the PI-3K/Akt pathway, for SK-induced cell survival, and for the changes in the apoptosis-related proteins. Thus, raised intracellular SK activity induced a mol. involved in cell-cell interactions to augment cell survival through a PI-3K/Akt-dependent pathway. This is distinct from the activation of both PI-3K/Akt and mitogen-activated protein kinase (MAPK) pathways seen with exogenously added S1P. Cells overexpressing SK showed enhanced survival under conditions of serum deprivation and absence of attachment to extracellular matrix, suggesting a role for SK in the regulation of vascular phenomena that occur under conditions of stress, such as angiogenesis and survival in unattached states, as would be required for a circulating endothelial cell.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:367261 HCAPLUS

DOCUMENT NUMBER: 142:427322

TITLE: Sphingosine kinase 1 is involved in dibutyryl cyclic AMP-induced granulocytic differentiation through the upregulation of extracellular signal-regulated kinase, but not p38 MAP kinase, in HL60 cells

AUTHOR(S): Koda, Masahiro; Murate, Takashi; Wang, Shulin; Ohguchi, Kenji; Sobue, Sayaka; Ikeda, Mika; Tamiya-Koizumi, Keiko; Igarashi, Yasuyuki; Nozawa, Yoshinori; Banno, Yoshiko

CORPORATE SOURCE: Department of Cell Signaling, Gifu University Graduate School of Medicine, Yanagido 1-1, Gifu, 501-1194, Japan

SOURCE: Biochimica et Biophysica Acta (2005), 1733(2-3), 101-110
CODEN: BBACAQ; ISSN: 0006-3002

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The role of sphingosine kinase (SPHK) in the dibutyryl cAMP (dbcAMP)-induced granulocytic differentiation of HL60 cells was investigated. During differentiation, SPHK activity was increased, as were mRNA and protein levels of SPHK1, but not of SPHK2. Pretreatment of HL60 cells with N,N-dimethylsphingosine (DMS), a potent SPHK inhibitor, completely blocked dbcAMP-induced differentiation. The phosphorylation of mitogen-activated protein kinases (MAPKs), extracellular signal-regulated kinase 1/2 (ERK1/2), and p38 MAPK was also increased during dbcAMP-induced differentiation. Pretreatment of HL60 cells with the MEK inhibitor, U0126, but not the p38 MAPK inhibitor, SB203580, completely suppressed dbcAMP-induced ERK1/2 activation and granulocytic differentiation, but did not affect the increase in SPHK activity. DMS inhibited dbcAMP-induced ERK1/2 activation, but had little effect on p38 MAPK activation. DMS had no effect on the dbcAMP-induced membrane translocation of protein kinase C (PKC) isoenzymes, and PKC inhibitors had no significant effect on ERK activation. The overexpression of wild-type SPHK1, but not dominant neg. SPHK1, resulted in high basal levels of ERK1/2 phosphorylation and

stimulated granulocytic differentiation in HL60 cells. These data show that SPHK1 participates in the dbcAMP-induced differentiation of HL60 cells by activating the MEK/ERK pathway.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:38370 HCAPLUS
DOCUMENT NUMBER: 142:91038
TITLE: Phosphorylation-dependent translocation of sphingosine kinase to the plasma membrane drives its oncogenic signalling
AUTHOR(S): Pitson, Stuart M.; Xia, Pu; Leclercq, Tamara M.; Moretti, Paul A. B.; Zebol, Julia R.; Lynn, Helen E.; Wattenberg, Binks W.; Vadas, Mathew A.
CORPORATE SOURCE: Hanson Institute and Division of Human Immunology, Institute of Medical and Veterinary Science, Adelaide, SA 5000, Australia
SOURCE: Journal of Experimental Medicine (2005), 201(1), 49-54
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sphingosine kinase (SK) 1 catalyzes the formation of the bioactive lipid sphingosine 1-phosphate, and was implicated in several biol. processes in mammalian cells, including enhanced proliferation, inhibition of apoptosis, and oncogenesis. Human SK (hSK) 1 possesses high intrinsic catalytic activity which can be further increased by a diverse array of cellular agonists. We have shown previously that this activation occurs as a direct consequence of extracellular signal-regulated kinase 1/2-mediated phosphorylation at Ser225, which not only increases catalytic activity, but is also necessary for agonist-induced translocation of hSK1 to the plasma membrane. In this study, the authors report that the oncogenic effects of overexpressed hSK1 are blocked by mutation of the phosphorylation site despite the phosphorylation-deficient form of the enzyme retaining full intrinsic catalytic activity. This indicates that oncogenic signaling by hSK1 relies on a phosphorylation-dependent function beyond increasing enzyme activity. We demonstrate, through constitutive localization of the phosphorylation-deficient form of hSK1 to the plasma membrane, that hSK1 translocation is the key effect of phosphorylation in oncogenic signaling by this enzyme. Thus, phosphorylation of hSK1 is essential for oncogenic signaling, and is brought about through phosphorylation-induced translocation of hSK1 to the plasma membrane, rather than from enhanced catalytic activity of this enzyme.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 54 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:431291 BIOSIS
DOCUMENT NUMBER: PREV200400435848
TITLE: Mammalian sphingosine kinase type 2 isoforms, cloning, expression and methods of use thereof.
AUTHOR(S): Spiegel, Sarah [Inventor, Reprint Author]; Kohama, Takafumi [Inventor]
CORPORATE SOURCE: McLean, VA, USA
ASSIGNEE: Sankyo Company, Ltd., Tokyo, Japan; Georgetown University
PATENT INFORMATION: US 6800470 20041005
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct 5 2004) Vol. 1287, No. 1. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent

LANGUAGE: English
ENTRY DATE: Entered STN: 10 Nov 2004
Last Updated on STN: 10 Nov 2004

AB Nucleic acids encoding mouse and **human sphingosine kinase** type 2 isoforms, methods for detecting agents or drugs which inhibit or promote sphingosine activity and therapeutic agents containing peptides or antibodies to peptides encoded by such nucleic acids.

L4 ANSWER 6 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:533806 HCAPLUS
DOCUMENT NUMBER: 141:84623
TITLE: Use of yeast DPL1, LCB4, and YSR2 mutants expressing heterologous sphingolipid pathway enzyme gene in screening for modulators of sphingolipid metabolism and/or signaling
INVENTOR(S): Saba, Julie D.
PATENT ASSIGNEE(S): Children's Hospital and Research Institute at Oakland, USA
SOURCE: U.S. Pat. Appl. Publ., 101 pp., Cont.-in-part of U.S. Ser. No. 348,052.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004126834	A1	20040701	US 2003-622011	20030716
US 2003175939	A1	20030918	US 2002-53510	20020117
US 6830881	B2	20041214		
US 2003219782	A1	20031127	US 2003-348052	20030117
PRIORITY APPLN. INFO.:			US 2002-349582P	P 20020117
			US 2002-53510	A2 20020117
			US 2003-348052	A2 20030117
			US 1997-939309	A2 19970929
			US 1999-356643	A2 19990719

AB A method for screening for agents that modulate sphingolipid metabolism and/or signaling pathways comprises culturing of yeast mutants in sphingosine-1-phosphate lyase gene DPL1, sphingosine kinase gene LCB4, and/or sphingosine-1-phosphate phosphatase gene YSR2 which express a nonendogenous sphingolipid pathway enzyme gene (such as human SPHK1) in presence of sphingosine and test compound Increased yeast growth in the presence of a test compound indicates the presence of a inhibitor of sphingolipid metabolism Thus, significant accumulation of phosphorylated sphingolipids in S. cerevisiae caused cell death. Yeast with defects in sphingolipid metabolism expressing **human sphingosine kinase** could therefore survive in the presence of inhibitors of the human enzyme.

L4 ANSWER 7 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1086668 HCAPLUS
DOCUMENT NUMBER: 142:49599
TITLE: Sphingosine Kinase 1 (SPHK1) Is Induced by Transforming Growth Factor-β and Mediates TIMP-1 Up-regulation
AUTHOR(S): Yamanaka, Masayoshi; Shegogue, Daniel; Pei, Heuping; Bu, Shizhong; Bielawska, Alicja; Bielawski, Jacek; Pettus, Benjamin; Hannun, Yusuf A.; Obeid, Lina; Trojanowska, Maria
CORPORATE SOURCE: Division of Rheumatology and Immunology and the

Department of Biochemistry and Molecular Biology, Medical University of South Carolina, and the Division of General Internal Medicine, Ralph H. Johnson Veterans Affairs Hospital, Charleston, SC, 29425, USA

SOURCE: Journal of Biological Chemistry (2004), 279(52), 53994-54001
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Transforming growth factor-β (TGF-β) signaling plays a pivotal role in extracellular matrix deposition by stimulating collagen production and other extracellular matrix proteins and by inhibiting matrix degradation The present study was undertaken to define the role of sphingosine kinase (SphK) in TGF-β signaling. TGF-β markedly up-regulated SphK1 mRNA and protein amts. and caused a prolonged increase in SphK activity in dermal fibroblasts. Concomitantly, TGF-β reduced sphingosine-1-phosphate phosphatase activity. Consistent with the changes in enzyme activity, corresponding changes in sphingolipid levels were observed such that sphingosine 1-phosphate (S1P) was increased (.apprx.2-fold), whereas sphingosine and ceramide were reduced after 24 h of TGF-β treatment. Given the relatively early induction of SphK gene expression in response to TGF-β, we examined whether SphK1 may be involved in the regulation of TGF-β-inducible genes that exhibit compatible kinetics, e.g. tissue inhibitor of metalloproteinase-1 (TIMP-1). We demonstrate that decreasing SphK1 expression by small interfering RNA (siRNA) blocked TGF-β-mediated up-regulation of TIMP-1 protein suggesting that up-regulation of SphK1 contributes to the induction of TIMP-1 in response to TGF-β. The role of SphK1 as a pos. regulator of TIMP-1 gene expression was further corroborated by using ectopically expressed SphK1 in the absence of TGF-β. Adenovirally expressed SphK1 led to a 2-fold increase of endogenous S1P and to increased TIMP-1 mRNA and protein production In addition, ectopic SphK1 and TGF-β cooperated in TIMP-1 up-regulation. Mechanistically, expts. utilizing TIMP-1 promoter constructs demonstrated that the action of SphK1 on the TIMP-1 promoter is through the AP1-response element, consistent with the SphK1-mediated up-regulation of phospho-c-Jun levels, a key component of AP1. Together, these expts. demonstrate that SphK/S1P are important components of the TGF-β signaling pathway involved in up-regulation of the TIMP-1 gene.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:858573 HCAPLUS

DOCUMENT NUMBER: 141:378597

TITLE: Anaphylatoxin Signaling in Human Neutrophils: A Key Role for Sphingosine Kinase

AUTHOR(S): Ibrahim, Farazeela Bte Mohd; Pang, See Jay; Melendez, Alirio J.

CORPORATE SOURCE: Department of Physiology, National University of Singapore, 117597, Singapore

SOURCE: Journal of Biological Chemistry (2004), 279(43), 44802-44811
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Anaphylatoxins activate immune cells to trigger the release of

proinflammatory mediators that can lead to the pathol. of several immune-inflammatory diseases. However, the intracellular signaling pathways triggered by anaphylatoxins are not well understood. Here the authors report for the first time that sphingosine kinase (SPHK) plays a key role in C5a-triggered signaling, leading to physiol. responses of human neutrophils. The authors demonstrate that C5a rapidly stimulates SPHK activity in neutrophils and differentiated HL-60 cells. Using the SPHK inhibitor N,N-dimethylsphingosine (DMS), the authors show that inhibition of SPHK abolishes the Ca2+ release from internal stores without inhibiting phospholipase C or protein kinase C activation triggered by C5a but has no effect on calcium signals triggered by other stimuli (FcγRII). The authors also show that DMS inhibits degranulation, activation of the NADPH oxidase, and chemotaxis triggered by C5a. Moreover, an antisense oligonucleotide against SPHK1, in neutrophil-differentiated HL-60 cells, had similar inhibitory properties as DMS, suggesting that the SPHK utilized by C5a is SPHK1. The authors' data indicate that C5a stimulation decreases cellular sphingosine levels and increases the formation of sphingosine-1-phosphate. Exogenously added sphingosine has a dual effect on C5a-stimulated oxidative burst: it has a priming effect at lower concns. but a dose-dependent inhibitory effect at higher concns.; however, C5a-triggered protein kinase C activity was only reduced at high concentration of sphingosine. In contrast, C5a-triggered Ca2+ signals, chemotaxis, and degranulation were not affected by sphingosine at all. Exogenous sphingosine-1-phosphate, by itself, did not induce degranulation or chemotaxis, but it did marginally induce Ca2+ signals and oxidative burst and had a priming effect, enhancing all the C5a-triggered responses. Taken together, these results suggest that SPHK plays an important role in the immune-inflammatory pathologies triggered by anaphylatoxins in human neutrophils and point out SPHK as a potential therapeutic target for the treatment of diseases associated with neutrophil hyperactivation.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:582001 HCAPLUS

DOCUMENT NUMBER: 141:155786

TITLE: Antisense Knockdown of Sphingosine Kinase 1 in Human Macrophages Inhibits C5a Receptor-Dependent Signal Transduction, Ca2+ Signals, Enzyme Release, Cytokine Production, and Chemotaxis

AUTHOR(S): Melendez, Alirio J.; Ibrahim, Farazeela Bte Mohd

CORPORATE SOURCE: Department of Physiology, National University of Singapore, Singapore, Singapore

SOURCE: Journal of Immunology (2004), 173(3), 1596-1603
CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The anaphylatoxin C5a is produced following the activation of the complement system and is associated with a variety of pathologies, including septic shock and adult respiratory distress syndrome, and with immune complex-dependent diseases such as rheumatoid arthritis. C5a has been shown to regulate inflammatory functions by interacting with its receptor, C5aR, which belong to the rhodopsin family of seven-transmembrane GPCRs. However, the intracellular signaling pathways triggered by C5aR on immune-effector cells are not well understood. In this report the authors present data showing that, in human monocyte-derived macrophages, C5aR uses the intracellular signaling mol. sphingosine kinase (SPHK)1 to trigger various physiol. responses. The authors' data show that C5a rapidly stimulates the generation of sphingosine-1-phosphate, SPHK activity, and membrane translocation of SPHK1. Using an antisense

oligonucleotide against SPHK1, the authors show that knockdown of SPHK1 abolishes the C5a-triggered intracellular Ca2+ signals, degranulation, cytokine generation, and chemotaxis. The authors' study shows for the first time that SPHK1 not only plays a key role in the generation and release of proinflammatory mediators triggered by anaphylatoxins from human macrophages but is also involved in the process of immune cell motility, thus pointing out SPHK1 as a potential therapeutic target for the treatment of inflammatory and autoimmune diseases.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:912420 HCAPLUS
DOCUMENT NUMBER: 141:393902
TITLE: Sphingosine kinase-1 mediates TNF-α-induced MCP-1 gene expression in endothelial cells: Upregulation by oscillatory flow
AUTHOR(S): Chen, Xi-Lin; Grey, Janice Y.; Thomas, Suzanne; Qiu, Fei-Hua; Medford, Russell M.; Wasserman, Martin A.; Kunsch, Charles
CORPORATE SOURCE: Discovery Research, AtheroGenics, Alpharetta, GA, 30004, USA
SOURCE: American Journal of Physiology (2004), 287(4, Pt. 2), H1452-H1458
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Atherosclerosis is a focal inflammatory disease and preferentially occurs in areas of low fluid shear stress and oscillatory flow, whereas the risk of atherosclerosis is decreased in regions of high fluid shear stress and steady laminar flow. Sphingosine kinase-1 (SphK1) catalyzes the conversion of sphingosine to sphingosine-1 phosphate (S1P), a sphingolipid metabolite that plays important roles in angiogenesis, inflammation, and cell growth. In the present study, we demonstrated that exposure of human aortic endothelial cells to oscillatory flow (shear stress, ±5 dyn/cm2 for 48 h) resulted in a marked increase in SphK1 mRNA levels compared with endothelial cells kept in static culture. In contrast, laminar flow (shear stress, 20 dyn/cm2 for 48 h) decreased SphK1 mRNA levels. We further investigated the role of SphK1 in TNF-α-induced expression of inflammatory genes, such as monocyte chemoattractant protein-1 (MCP-1) and VCAM-1 by using small interfering RNA (siRNA) specifically for SphK1. Treatment of endothelial cells with SphK1 siRNA suppressed TNF-α-induced increase in MCP-1 mRNA levels, MCP-1 protein secretion, and activation of p38 MAPK. SphK1 siRNA also inhibited TNF-α-induced cell surface expression of VCAM-1, but not ICAM-1, protein. Exposure of endothelial cells to S1P led to an increase in MCP-1 protein secretion and MCP-1 mRNA levels and activation of NF-κB-mediated transcriptional activity. Treatment of endothelial cells with the p38 MAPK inhibitor SB-203580 suppressed S1P-induced MCP-1 protein secretion. These data suggest that SphK1 mediates TNF-α-induced MCP-1 gene expression through a p38 MAPK-dependent pathway and may participate in oscillatory flow-mediated proinflammatory signaling pathway in the vasculature.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 54 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:44696 SCISEARCH
THE GENUINE ARTICLE: 881YT
TITLE: Identification of genetic and epigenetic similarities of SPHK1/Sphk1 in mammals

AUTHOR: Imamura T; Miyauchi-Senda N; Tanaka A; Shiota K (Reprint)
CORPORATE SOURCE: Univ Tokyo, Lab Cellular Biochem, Bunkyo Ku, 1-1-1 Yayoi, Tokyo 1138657, Japan (Reprint); Univ Tokyo, Lab Cellular Biochem, Bunkyo Ku, Tokyo 1138657, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: JOURNAL OF VETERINARY MEDICAL SCIENCE, (NOV 2004) Vol. 66, No. 11, pp. 1387-1393.
Publisher: JAPAN SOC VET SCI, UNIV TOKYO, 1-1-1 YAYOI, BUNKYO-KU, TOKYO, 103, JAPAN.
ISSN: 0916-7250.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 37

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In normal tissues, methylation of CpG islands is generally accepted to be limited to the inactive X-chromosome and imprinting clusters. Gene Sphk1 has shown complex organization, indicated by multiple alternative splicing and tissue-dependent DNA methylation within the limited area (T-DMR) of the CpG island in the rat. Comparisons among human, mouse and rat SPHK1/Sphk1 genomic DNA revealed five coding exons and association of a CpG island at the 5' end in common. We also found two novel subtypes, for a total of eight mRNA subtypes generated through selective usage of untranslated first exons. A 38-bp region at the 5'-end of T-DMR is highly conserved. This restricted area is specifically hypomethylated in the brain. Here, we examine the complex genetic/epigenetic features of the SPHK1/Sphk1 CpG island, and suggest that the T-DMR is the core target for tissue-dependent CpG island methylation.

L4 ANSWER 12 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:488029 HCAPLUS
DOCUMENT NUMBER: 141:104338
TITLE: Sphingosine kinase mediates activation of extracellular signal-related kinase and Akt by respiratory syncytial virus
AUTHOR(S): Monick, Martha M.; Cameron, Kelli; Powers, Linda S.; Butler, Noah S.; McCoy, Diann; Mallampalli, Rama K.; Hunninghake, Gary W.
CORPORATE SOURCE: University of Iowa Roy J. and Lucille A. Carver College of Medicine, Iowa City, IA, USA
SOURCE: American Journal of Respiratory Cell and Molecular Biology (2004), 30(6), 844-852
CODEN: AJRBEL; ISSN: 1044-1549
PUBLISHER: American Thoracic Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Respiratory syncytial virus (RSV) preferentially infects lung epithelial cells. Infected cells remain viable well into the infection. This prolonged survival results from RSV-induced activation of pro-survival pathways, including Akt and extracellular signal-related kinase (ERK). Sphingosine 1-phosphate (S1P) is a sphingolipid metabolite with demonstrated links to cell survival. It is enzymically generated by sequential activation of ceramidase (generation of sphingosine) and sphingosine kinase (generation of S1P). In these studies, it was found that RSV stimulated neutral ceramidase and sphingosine kinase activities in lung epithelial cells. The combined effect of activation of these two enzymes would decrease proapoptotic ceramide and increase antiapoptotic S1P. S1P activated Akt and ERK within minutes, and inhibition of sphingosine kinase blocked RSV-induced ERK and Akt activation, leading to accelerated cell death after viral infection. RSV infection does eventually kill infected cells but activation of cell survival pathways significantly delays cell death. The studies are the first evidence linking sphingolipid metabolites to cell survival mechanisms in the context of a viral infection.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 54 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:419584 BIOSIS
DOCUMENT NUMBER: PREV200400420092
TITLE: Genomic organization and mutation analysis of three candidate genes for hereditary neuralgic amyotrophy.
AUTHOR(S): Honermund, Gert; Schirmacher, Anja; Ringelstein, Bernd; Young, Peter; Watts, Giles D.; Meuleman, Jan; Nelis, Eva; Chance, Phillip F.; Timmerman, Vincent; Stogbauer, Florian; Kuhlenbaumer, Gregor [Reprint Author]
CORPORATE SOURCE: Dept Neurol, Univ Munster, Albert Schweitzer Str 33, D-48129, Munster, Germany
gkuhlen@uni-muenster.de
SOURCE: Muscle & Nerve, (April 2004) Vol. 29, No. 4, pp. 601-604. print.
CODEN: MUNEDE. ISSN: 0148-639X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Nov 2004
Last Updated on STN: 3 Nov 2004
AB Hereditary neuralgic amyotrophy (HNA) is an autosomal-dominant inherited recurrent focal neuropathy affecting mainly the brachial plexus. In this study we report the genomic structure and mutation analysis of three candidate genes: sphingosine kinase 1 (SPHK1); tissue inhibitor of metalloproteinase 2 (TIMP2); and cytoglobin (CYGB). We did not find any disease-associated mutations, indicating that HNA is not caused by point mutations in these genes. However, we identified several sequencing errors in the cDNA of SPHK1 as well as seven novel single-nucleotide polymorphisms.

L4 ANSWER 14 OF 54 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 1
ACCESSION NUMBER: 2005:202804 BIOSIS
DOCUMENT NUMBER: PREV200500200384
TITLE: Expression of the **human sphingosine kinases** (huSPHKs) in the yeast saccharomyces cerevisiae.
AUTHOR(S): Grosz, Gabor [Reprint Author]; Takacs, Laszlo; Feher, Zsigmond
CORPORATE SOURCE: Med and Hlth Sci CtrDept Human Genet, Univ Debrecen, Debrecen, Hungary
SOURCE: Tissue Antigens, (October 2004) Vol. 64, No. 4, pp. 415. print.
Meeting Info.: 1st International Conference on Basic and Clinical Immunogenomics. Budapest, Hungary. October 03-07, 2004. Hungarian Society for Immunology; Foundation of Inflammation Biology Research; Diamond Congress Ltd.
CODEN: TSANA2. ISSN: 0001-2815.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Jun 2005
Last Updated on STN: 1 Jun 2005

L4 ANSWER 15 OF 54 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004342307 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15246004
TITLE: An assay for sphingosine kinase activity using biotinylated sphingosine and streptavidin-coated membranes.
AUTHOR: Roberts Jane L; Moretti Paul A B; Darrow Andrew L; Derian

Claudia K; Vadas Mathew A; Pitson Stuart M
CORPORATE SOURCE: Hanson Institute, Division of Human Immunology, Institute of Medical and Veterinary Science, Frome Road, Adelaide, SA 5000, Australia.
SOURCE: Analytical biochemistry, (2004 Aug 1) 331 (1) 122-9. Journal code: 0370535. ISSN: 0003-2697.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 20040713
Last Updated on STN: 20050129
Entered Medline: 20050128

AB Sphingosine kinase catalyses the phosphorylation of sphingosine to generate sphingosine 1-phosphate, a lipid signaling molecule implicated in roles in a diverse range of mammalian cell processes through its action as both a ligand for G-protein-coupled cell-surface receptors and an apparent intracellular second messenger. This paper describes a rapid, sensitive, and reproducible assay for sphingosine kinase activity using biotinylated sphingosine (biotinyl-Sph) as a substrate and capturing the phosphorylated product with streptavidin-coated membranes. We have shown that both **human sphingosine kinase** 1 and 2 (hSK1 and hSK2) can efficiently phosphorylate biotinyl-Sph, with K(m) values similar to those of sphingosine. The assay utilizing this substrate has high sensitivity for hSK1 and hSK2, with detection limits in the low-femtomole range for both purified recombinant enzymes. Importantly, we have also demonstrated the capacity of this assay to measure endogenous sphingosine kinase activity in crude cell extracts and to follow changes in this activity following sphingosine kinase activation. Together, these results demonstrate the potential utility of this assay in both cell-based analysis of sphingosine kinase signaling pathways and high-throughput screens for agents affecting sphingosine kinase activity in vitro.

L4 ANSWER 16 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1088713 HCAPLUS
DOCUMENT NUMBER: 142:234772
TITLE: Sphingosine kinase activity confers resistance to apoptosis by fumonisin B1 in human embryonic kidney (HEK-293) cells
AUTHOR(S): Sharma, Neelesh; He, Quanren; Sharma, Raghubir P.
CORPORATE SOURCE: Department of Physiology and Pharmacology, College of Veterinary Medicine, The University of Georgia, Athens, GA, 30602-7389, USA
SOURCE: Chemico-Biological Interactions (2004), 151(1), 33-42 CODEN: CBINA8; ISSN: 0009-2797
PUBLISHER: Elsevier Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fumonisin B1 induces cytotoxicity in sensitive cells by inhibiting ceramide synthase due to its structural similarity to the long-chain backbones of sphingolipids. The resulting accumulation of sphingoid bases was established as a mechanism for fumonisin B1 cytotoxicity. We found that despite the accumulation of sphinganine, human embryonic kidney (HEK-293) cells are resistant to fumonisin B1 toxicity; 25 μM fumonisin B1 exposure for 48 h did not increase apoptosis in these cells, while it did so in sensitive porcine kidney epithelial (LLC-PK1) cells. In this study, DL-threo-dihydrosphingosine, the sphingosine kinase inhibitor (SKI), considerably increased the sensitivity of HEK-293 cells to fumonisin B1. Treatment of these cells with 25 μM fumonisin B1 and 2.5 μM SKI increased apoptosis. Sphingoid bases, sphinganine or sphingosine, added to cell cultures induced apoptosis by themselves and their effects were potentiated by SKI or fumonisin B1. Addition of physiol.

amts. of sphingosine-1-phosphate prevented the toxic effects induced by SKI inhibition and fumonisin B1. Results indicated that HEK-293 cells are resistant to fumonisin B1 due to rapid formation of sphingosine-1-phosphate that imparts survival properties. Taken together, these findings suggest that sphingoid base metabolism by sphingosine kinase may be a critical event in rendering the HEK-293 cells relatively resistant to fumonisin B1-induced apoptosis.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:1006765 HCAPLUS
DOCUMENT NUMBER: 140:35992
TITLE: Sphingosine kinase inhibitors and their therapeutic use
INVENTOR(S): Smith, Charles D.; French, Kevin J.; Yun, Jong K.
PATENT ASSIGNEE(S): The Pennsylvania State Research Foundation, USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003105840	A2	20031224	WO 2003-US19162	20030617
WO 2003105840	A3	20040325		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004034075	A1	20040219	US 2003-462954	20030617
PRIORITY APPLN. INFO.:			US 2002-432511P P	20020617

OTHER SOURCE(S): MARPAT 140:35992
AB The invention discloses compds., compns. and methods for inhibiting sphingosine kinase and for treating or preventing hyperproliferative disease, autoimmune disease, inflammatory disease, or allergy. Antitumor activity of e.g. 2-(3,4-dihydroxybenzylidene)benzofuran-3-one (preparation included) is described.

L4 ANSWER 18 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:796515 HCAPLUS
DOCUMENT NUMBER: 139:303797
TITLE: Variants of mammalian sphingosine kinase with reduced catalytic activity and their use in controlling sphingosine-1-phosphate activated processes
INVENTOR(S): Pitson, Stuart M.; Xia, Pu; Moretti, Paul A.; Verwey, Julia R.; Vadas, Mathew A.; Wattenberg, Brian W.
PATENT ASSIGNEE(S): Medvet Science Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082322	A1	20031009	WO 2003-AU388	20030328
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ; TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2480661	AA	20031009	CA 2003-2480661	20030328
EP 1499343	A1	20050126	EP 2003-745226	20030328
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:

AU 2002-1448	A	20020328
AU 2002-1538	A	20020405
AU 2002-1621	A	20020408
AU 2002-951668	A	20020919
AU 2003-900230	A	20030121
WO 2003-AU388	W	20030328

AB The present invention relates generally to a method of modulating cellular activity by modulating the activity of sphingosine kinase by modulating phosphorylation of the enzyme. Modulating phosphorylation of the enzyme modulates the activity of the enzyme and its ability to catalyze formation of the signaling mol. sphingosine-1-phosphate. The present invention still further extends to sphingosine kinase variants and to functional derivs., homologues or analogs, chemical equivalent and mimetics thereof exhibiting reduced and/or ablated capacity to undergo phosphorylation. The method and mols. of the present invention are useful, inter alia, in the treatment and/or prophylaxis of conditions characterized by aberrant, unwanted or otherwise inappropriate cellular and/or sphingosine kinase functional activity. The present invention is further directed to methods for identifying and/or designing agents capable of modulating sphingosine kinase phosphorylation.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:335288 HCAPLUS
DOCUMENT NUMBER: 138:349758
TITLE: DNA sequence of promoter for **human sphingosine kinase** 1 and uses
INVENTOR(S): Kohama, Takafumi; Sugiura, Masako
PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003035871	A1	20030501	WO 2002-JP10882	20021021
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,				

UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

JP 2003199590 A2 20030715 JP 2002-307956 20021023
PRIORITY APPLN. INFO.: JP 2001-325402 A 20011023

AB This invention provides DNA sequence of promoter for **human sphingosine kinase** 1. The expression level of reporter gene was enhanced when the expression was regulated under sphingosine kinase 1 promoter. The promoter provided in this invention can be used for diagnosis, treatment and screening the drugs for arteriosclerosis, diabetes, thrombosis, inflammation, immunopathy, allergy, cancer and cancer metastasis.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:301229 HCAPLUS
DOCUMENT NUMBER: 138:316762
TITLE: **Human sphingosine kinase** 3, encoding cDNA, and use in drug screening and diagnosis
INVENTOR(S): Igarashi, Yasuyuki; Kihara, Akio
PATENT ASSIGNEE(S): Hokkaido Technology Licensing Office Co., Ltd., Japan; Chemical Biology Institute
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003031628	A1	20030417	WO 2001-JP8538	20010928

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2001-JP8538 20010928

AB Human secretory sphingosine kinase 3 (SPHK3), cDNA encoding it, recombinant expression, and use in drug screening for and diagnosis of sphingosine-related diseases, are disclosed. A novel sphingosine kinase was purified from human and its amino acid sequence determined Its cDNA was cloned and expressed in COS-7 cells. Besides phosphorylating sphingosine to produce sphingosine-1-phosphate, it also acts on D-erythro-dihydrosphingosine, N,N-dimethyl-sphingosine, diacylglycerol, and phosphatidylinositol.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:301228 HCAPLUS
DOCUMENT NUMBER: 138:316761
TITLE: Sphingosine kinase 4 from human platelet, encoding cDNA, and use in drug screening and diagnosis

INVENTOR(S): Igarashi, Yasuyuki; Kihara, Akio
PATENT ASSIGNEE(S): Hokkaido Technology Licensing Office Co., Ltd., Japan; Chemical Biology Institute
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003031627	A1	20030417	WO 2001-JP8537	20010928

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2001-JP8537 20010928

AB Human platelet-origin sphingosine kinase 4 (SPHK4), cDNA encoding it, recombinant expression, and use in drug screening for and diagnosis of sphingosine-related diseases, are disclosed. A novel sphingosine kinase was purified from human platelet and its amino acid sequence determined Its cDNA was cloned and expressed in E. coli.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:76920 HCAPLUS
DOCUMENT NUMBER: 138:132230
TITLE: RPK118, a novel **human sphingosine kinase**-1-binding protein
INVENTOR(S): Nakamura, Shunichi; Okada, Taro
PATENT ASSIGNEE(S): The New Industry Research Organization, Japan
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008582	A1	20030130	WO 2002-JP7352	20020719

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2001-220516 A 20010719

AB A novel sphingosine kinase 1-binding protein RPK118 isolated from human brain, its encoding cDNA, and recombinant expression, are disclosed.

Probes and antibodies are claimed. Sphingosine kinase (SPHK) is a key enzyme catalyzing the formation of sphingosine 1 phosphate (SPP), a lipid messenger that is implicated in the regulation of a wide variety of important cellular events through intracellular as well as extracellular mechanisms. However, the mol. mechanism of the intracellular actions of SPP remains unclear. Here the authors have cloned a novel sphingosine kinase-1 (SPHK1)-binding protein, RPK118, by yeast two-hybrid screening. RPK118 contains several functional domains whose sequences are homologous to other known proteins including the phox homol. domain and pseudokinase 1 and 2 domains and is shown to be a member of an evolutionarily highly conserved gene family. The pseudokinase 2 domain of RPK118 is responsible for SPHK1 binding as judged by yeast two-hybrid screening and immunopptn. studies. RPK118 is also shown to co-localize with SPHK1 on early endosomes in COS7 cells expressing both recombinant proteins. Furthermore, RPK118 specifically binds to phosphatidylinositol 3-phosphate. RPK118 binds to sphingosine kinase 1 in the C-terminal side of the P-kinase domain and transports sphingosine kinase 1 to a specific site in a cell via the PX domain and the ESP domain, thereby serving as a sorting protein. These results strongly suggest that RPK118 is a novel SPHK1-binding protein that may be involved in transmitting SPP-mediated signaling into the cell.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:896727 HCAPLUS

DOCUMENT NUMBER: 140:74609

TITLE: Sphingosine Kinase 2 is a Nuclear Protein and Inhibits DNA Synthesis

AUTHOR(S): Igarashi, Nobuaki; Okada, Taro; Hayashi, Shun; Fujita, Toshitada; Jahangeer, Saleem; Nakamura, Shun-Ichi

CORPORATE SOURCE: Department of Molecular and Cellular Biology, Division of Biochemistry, Kobe University Graduate School of Medicine, Kobe, 650-0017, Japan

SOURCE: Journal of Biological Chemistry (2003), 278(47), 46832-46839
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Sphingosine kinase-1 (SPHK1) is a key enzyme catalyzing the formation of an important bioactive lipid messenger, sphingosine 1-phosphate, and is implicated in the regulation of cell proliferation and antiapoptotic processes. Biol. features of another isoenzyme SPHK2, however, remain unclear. The present studies were undertaken to characterize SPHK2 by comparison with SPHK1. When SPHK2 was transiently expressed in various cell lines, it was localized in the nuclei as well as in the cytosol, whereas SPHK1 was distributed in the cytosol but not in the nucleus. The authors have mapped a functional nuclear localization signal (NLS) to the N-terminal region of SPHK2. The authors have observed that the expression of SPHK2 in various cell types causes inhibition of DNA synthesis, resulting in the cell cycle arrest at G1/S phase. The authors have also demonstrated that an NLS mutant of SPHK2, SPHK2R93E/R94E, failed to enter the nucleus and to inhibit DNA synthesis. Moreover, a fusion protein, NLS-SPHK1, where SPHK1 was fused to the NLS sequence of SPHK2 acquired the ability to enter nuclei and inhibited DNA synthesis. These results indicate that SPHK2 localizes in the nuclei and causes inhibition of DNA synthesis, and this may affect subsequent cellular events.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 54 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2003460343 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14522923
TITLE: Discovery and evaluation of inhibitors of **human sphingosine kinase**.
AUTHOR: French Kevin J; Schrecengost Randy S; Lee Brian D; Zhuang Yan; Smith Staci N; Eberly Justin L; Yun Jong K; Smith Charles D
CORPORATE SOURCE: Department of Pharmacology, Penn State College of Medicine, Hershey, Pennsylvania 17033, USA.
CONTRACT NUMBER: R24 CA788243 (NCI)
SOURCE: Cancer research, (2003 Sep 15) 63 (18) 5962-9. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20031003
Last Updated on STN: 20031218
Entered Medline: 20031204

AB Sphingolipid-metabolizing enzymes control the dynamic balance of the cellular levels of bioactive lipids, including the proapoptotic compound ceramide and the proliferative compound sphingosine 1-phosphate. Accumulating evidence indicates that sphingosine kinase (SK) plays a pivotal role in regulating tumor growth and that SK can act as an oncogene. Despite the importance of SK for cell proliferation, pharmacological inhibition of SK is an untested means of treating cancer because of the current lack of nonlipid inhibitors of this enzyme. To further assess the involvement of SK in human tumors, levels of RNA for SK in paired samples of cDNA prepared from tumors and normal adjacent tissue were analyzed. Expression of SK RNA was significantly elevated in a variety of solid tumors, compared with normal tissue from the same patient. To identify and evaluate inhibitors of SK, a medium throughput assay for recombinant human SK fused to glutathione S-transferase was developed, validated, and used to screen a library of synthetic compounds. A number of novel inhibitors of human SK were identified, and several representative compounds were characterized in detail. These compounds demonstrated activity at sub- to micromolar concentrations, making them more potent than any other reported SK inhibitor, and were selective toward SK compared with a panel of human lipid and protein kinases. Kinetic studies revealed that the compounds were not competitive inhibitors of the ATP-binding site of SK. The SK inhibitors were antiproliferative toward a panel of tumor cell lines, including lines with the multidrug resistance phenotype because of overexpression of either P-glycoprotein or multidrug resistance phenotype 1, and were shown to inhibit endogenous human SK activity in intact cells. Furthermore, each inhibitor induced apoptosis concomitant with tumor cell cytotoxicity. Methods for the synthesis of a series of aurone inhibitors of SK were established, and a prototypical dihydroxyaurone was found to have moderate antitumor activity in vivo in the absence of overt toxicity to the mice. These compounds are the first examples of nonlipid inhibitors of SK with in vivo antitumor activity and so provide leads for additional development of inhibitors of this important molecular target.

L4 ANSWER 25 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:318819 HCAPLUS
DOCUMENT NUMBER: 139:34620
TITLE: Sphingosine kinase-dependent migration of immature dendritic cells in response to neurotoxic prion protein fragment
AUTHOR(S): Kaneider, Nicole C.; Kaser, Arthur; Dunzendorfer, Stefan; Tilg, Herbert; Wiedermann, Christian J.

CORPORATE SOURCE: Division of General Internal Medicine, Department of Internal Medicine, University of Innsbruck, Innsbruck, A-6020, Austria
SOURCE: Journal of Virology (2003), 77(9), 5535-5539
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The concept that circulating dendritic cells mediate neuroinvasion in transmissible spongiform encephalopathies received strong support from recent observations that prion protein is expressed in myeloid dendritic cells. The authors observed that prion protein fragment 106-126 is a chemoattractant for monocyte-derived immature but not mature dendritic cells. Signaling events in chemotaxis involved enzymes downstream of Gq protein and were inhibited by blockade of sphingosine kinase, suggesting transactivation of sphingosine-1-phosphate-dependent cell motility by prion protein.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:810828 HCAPLUS
DOCUMENT NUMBER: 140:71238
TITLE: Sphingosine kinase transmits estrogen signaling in human breast cancer cells
AUTHOR(S): Sukocheva, Olga A.; Wang, Lijun; Albanese, Nathaniel; Pitson, Stuart M.; Vadas, Mathew A.; Xia, Pu
CORPORATE SOURCE: Signal Transduction Laboratory, Division of Human Immunology, Hanson Institute, Institute of Medical and Veterinary Science and University of Adelaide, Adelaide, 5000, Australia
SOURCE: Molecular Endocrinology (2003), 17(10), 2002-2012
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Current understanding of cytoplasmic signaling pathways that mediate estrogen action in human breast cancer is incomplete. Here we report that treatment with 17β-estradiol (E2) activates a novel signaling pathway via activation of sphingosine kinase (SphK) in MCF-7 breast cancer cells. We found that E2 has dual actions to stimulate SphK activity, i.e. a rapid and transient activation mediated by putative membrane G protein-coupled estrogen receptors (ER) and a delayed but prolonged activation relying on the transcriptional activity of ER. The E2-induced SphK activity consequently activates downstream signal cascades including intracellular Ca2+ mobilization and Erk1/2 activation. Enforced expression of human SphK type 1 gene in MCF-7 cells resulted in increases in SphK activity and cell growth. Moreover, the E2-dependent mitogenesis were highly promoted by SphK overexpression as determined by colony growth in soft agar and solid focus formation. In contrast, expression of SphKG82D, a dominant-neg. mutant SphK, profoundly inhibited the E2-mediated Ca2+ mobilization, Erk1/2 activity and neoplastic cell growth. Thus, our data suggest that SphK activation is an important cytoplasmic signaling to transduce estrogen-dependent mitogenic and carcinogenic action in human breast cancer cells.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 54 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:501633 BIOSIS
DOCUMENT NUMBER: PREV200300498069
TITLE: Discovery of high-affinity inhibitors of **human**

sphingosine kinase.

AUTHOR(S): French, Kevin J. [Reprint Author]; Schrecengost, Randy S.; Lee, Brian D.; Zhuang, Yan; Smith, Staci N.; Yun, Jong K.; Smith, Charles D.

CORPORATE SOURCE: Apogee Biotechnology Company, Hershey, PA, USA

SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (July 2003) Vol. 44, pp. 686. print.
Meeting Info.: 94th Annual Meeting of the American Association for Cancer Research. Washington, DC, USA. July 11-14, 2003.
ISSN: 0197-016X.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 29 Oct 2003
Last Updated on STN: 29 Oct 2003

L4 ANSWER 28 OF 54 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:1003240 SCISEARCH
THE GENUINE ARTICLE: 741TT

TITLE: Sphingosine-1-phosphate formation activates phosphatidylinositol-4 kinase in basolateral membranes from kidney cells: Crosstalk in cell signaling through sphingolipids and phospholipids

AUTHOR: Einicker-Lamas M; Wenceslau L D; Bernardo R R; Nogaroli L; Guilherme A; Oliveira M M; Vieyra A (Reprint)

CORPORATE SOURCE: Univ Fed Rio de Janeiro, Inst Biofis Carlos Chagas Filho, BR-21941590 Rio De Janeiro, Brazil (Reprint); Univ Massachusetts, Sch Med, Worcester, MA 01605 USA

COUNTRY OF AUTHOR: Brazil; USA

SOURCE: JOURNAL OF BIOCHEMISTRY, (OCT 2003) Vol. 134, No. 4, pp. 529-536.
Publisher: JAPANESE BIOCHEMICAL SOC, ISHIKAWA BLDG-3F, 25-16 HONGO-5-CHOME, BUNKYO-KU, TOKYO, 113, JAPAN.
ISSN: 0021-924X.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 66

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Sphingosine-1-phosphate (SIP) and phosphatidylinositol-4 phosphate [PtdIns(4)P] are important second messengers in various cellular processes. Here, we show that SIP and PtdIns(4)P are formed in purified basolateral membranes (BLM) derived from kidney proximal tubules, indicating the presence of a plasma membrane associated SPK (BLM-SPK) and phosphatidylinositol-4 kinase (PI-4K). We observed that SIP synthesis is linear with time, dependent on protein concentration, and saturable in the presence of increasing concentrations of sphingosine. Different from the observations on cytosolic SPKs, the formation of SIP by BLM-SPK is Mg2+-independent and insensitive to the classical inhibitor of the cytosolic SPKs, DL-threo-dihydrosphingosine. With sphingosine as substrate, the enzyme shows cooperative kinetics (n = 3.4) with a K-0.5 value of 0.12 mM, suggesting that BLM-SPK is different from the previously characterized cytosolic SPK. The formation of PtdIns(4)P markedly inhibits BLM-SPK activity. Conversely, a strong activation of PtdIns(4)P synthesis by the formation of SIP is observed. Taken together, these results indicate that (i) basolateral membranes from kidney cells harbor a SPK activity that potentially regulates renal epithelium function, and (ii) the formation of SIP mediated by SPK enhances PI-4K activity, while PtdIns(4)P in turn inhibits SPK, suggesting an interplay between these lipid signaling molecules. These findings suggest the possibility of crosstalk between sphingolipids and glycerolipids, which might be involved in the regulation of transepithelial fluxes across the BLM of kidney

cells.

L4 ANSWER 29 OF 54 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2003498617 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14575709
TITLE: Identification of functional nuclear export sequences in **human sphingosine kinase** 1.
AUTHOR: Inagaki Yuichi; Li Pei-Yun; Wada Atsushi; Mitsutake Susumu; Igarashi Yasuyuki
CORPORATE SOURCE: Department of Biomembrane and Biofunctional Chemistry, Graduate School of Pharmaceutical Sciences, Hokkaido University, Sapporo, Japan.
SOURCE: Biochemical and biophysical research communications, (2003 Nov 7) 311 (1) 168-73.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20031025
Last Updated on STN: 20040122
Entered Medline: 20040121

AB Sphingosine kinase (SPHK) is an enzyme that phosphorylates sphingosine to form sphingosine 1-phosphate (S1P). Human SPHK1 (hSPHK1) was localized predominantly in the cytoplasm when transiently expressed in Cos7 cells. In this study, we have found two functional nuclear export signal (NES) sequences in the middle region of hSPHK1. Deletion and mutagenesis studies revealed that the cytoplasmic localization of SPHK1 depends on its nuclear export, directed by the NES. Furthermore, upon treatment with leptomycin B, a specific inhibitor of the nuclear export receptor CRM1, a marked nuclear accumulation of hSPHK1 was observed, indicating that hSPHK1 shuttles between the cytoplasm and the nucleus. Our results provide the first evidence of the active nuclear export of SPHK1 and suggest it is mediated by a CRM1-dependent pathway.

L4 ANSWER 30 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:156649 HCAPLUS
DOCUMENT NUMBER: 139:50301
TITLE: Ca2+/calmodulin-dependent translocation of sphingosine kinase: Role in plasma membrane relocation but not activation
AUTHOR(S): Young, Kenneth W.; Willets, Jonathon M.; Parkinson, M. Janine; Bartlett, Paula; Spiegel, Sarah; Nahorski, Stefan R.; Challiss, R. A. John
CORPORATE SOURCE: Department of Cell Physiology and Pharmacology, University of Leicester, Leicester, LE1 9HN, UK
SOURCE: Cell Calcium (2003), 33(2), 119-128
CODEN: CECADV; ISSN: 0143-4160
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Activation of sphingosine kinase (SPHK), thereby increasing cellular levels of sphingosine 1-phosphate (S1P), may be involved in a variety of intracellular responses including Ca2+ signaling. This study uses mammalian SPHK1a, tagged with enhanced green fluorescent protein (eGFP), to examine whether translocation of this enzyme is linked with Ca2+-mobilizing responses. Real-time confocal imaging of SPHK1a-eGFP in human SH-SY5Y neuroblastoma cells visualized a relocation of the enzyme from the cytosol to the plasma membrane in response to Ca2--mobilizing stimuli (muscarinic M3- or lysophosphatidic acid receptor activation, and thapsigargin-mediated store release). This redistribution was preceded by a transient increase in cytosolic SPHK1a-eGFP levels due to liberation of

SPHK from localized higher intensity regions. Translocation was dependent on Ca2+ mobilization from intracellular stores, and was prevented by pretreatment with the Ca2+/calmodulin inhibitor W-7, but not W-5 or KN-62. In functional studies, pretreatment with W-7 lowered basal and M3-receptor-mediated cellular S1P production However, this pretreatment did not alter agonist-mediated Ca2+ responses, and SPHK1a-eGFP activity itself appeared insensitive to Ca2+/calmodulin and W-7. These data suggest a role for Ca2+/calmodulin in controlling the subcellular distribution but not the activity of SPHK1a.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 54 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:138843 BIOSIS
DOCUMENT NUMBER: PREV200400140829
TITLE: Regulation of sphingosine kinase 1 gene expression by protein kinase C in a human leukemia cell line, MEG-01.
AUTHOR(S): Nakade, Yusuke; Banno, Yoshiko; T-Koizumi, Keiko; Hagiwara, Kazumi; Sobue, Sayaka; Koda, Masahiro; Suzuki, Motoshi; Kojima, Tetsuhito; Takagi, Akira; Asano, Haruhiko; Nozawa, Yoshinori; Murate, Takashi [Reprint Author]
CORPORATE SOURCE: Graduate School of Medicine, School of Health Sciences, Nagoya University, Daiko-Minami 1-1-20, Higashi, 461-8673, Nagoya, Japan
murate@met.nagoya-u.ac.jp
SOURCE: Biochimica et Biophysica Acta, (30 December 2003) Vol. 1635, No. 2-3, pp. 104-116. print.
ISSN: 0006-3002 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Mar 2004
Last Updated on STN: 10 Mar 2004

AB The prolonged treatment with phorbol 12-myristate 13-acetate (PMA) of a human megakaryoblastic leukemia cell line, MEG-01, induced increase of sphingosine kinase (SPHK) enzyme activity and SPHK1 protein expression as well as SPHK1 message. Protein kinase C (PKC) inhibitor prevented the PMA-induced SPHK1 gene expression. To elucidate the regulatory mechanism of this gene expression, we examined the promoter area (distal to the first exon) and its binding proteins. Luciferase analyses showed that the area of 300 bp from the first exon was sufficient for PMA-responsiveness, and that specificity protein 1 (Sp1)- and two activator protein 2 (AP-2)-binding motifs within this area were necessary for responsiveness. Inhibitors for PKCTM and MEK1 decreased this PMA-induced promoter activity. Electrophoresis mobility shift assay (EMSA) showed that Sp1 protein was originally bound to the Sp1 site and that two additional bands bound to the two AP-2 motifs were observed only when stimulated with PMA in MEG-01 cells. The appearance of these bands resulted from binding to an unknown protein rather than AP-2. These results indicated that PMA up-regulates SPHK1 gene expression through PMA-responsive elements of the 5' promoter area of the gene, and suggested that PMA-mediated SPHK1 gene expression would be mediated via PKC- and ERK-dependent signal transduction pathway by binding the transcription factor to AP-2 motifs.

L4 ANSWER 32 OF 54 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
DUPLICATE 5

ACCESSION NUMBER: 2003-10480 BIOTECHDS
TITLE: Modulating cytokine- or tumor necrosis factor-induced cellular activity, useful for treating or preventing a neoplastic condition, comprises modulating an intracellular sphingosine kinase-dependent signaling mechanism;
protein-induced cellular activity modulation and agonist and antagonist for use in disease therapy

AUTHOR: XIA P; WANG L; VADAS M; GAMBLE J; MORETTI P; PITSON S
PATENT ASSIGNEE: MEDVET SCI PTY LTD
PATENT INFO: WO 2002098458 12 Dec 2002
APPLICATION INFO: WO 2002-AU710 3 Jun 2002
PRIORITY INFO: AU 2001-9759 27 Dec 2001; AU 2001-5521 7 Jun 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-201282 [19]
AB DERWENT ABSTRACT:
NOVELTY - Modulating cytokine-induced or tumor necrosis factor (TNF)-induced cellular activity, comprises contacting the cell with an agent under conditions sufficient to modulate the interaction of sphingosine kinase with a TNF receptor-associated factor (TRAF), preferably TRAF2, where inducing the association up-regulates cellular activity, and inhibiting the association down-regulates cellular activity.

DETAILED DESCRIPTION - Modulating cytokine-induced or tumor necrosis factor (TNF)-induced cellular activity, comprises contacting the cell with an agent for a time and under conditions sufficient to modulate the interaction of sphingosine kinase with a TNF receptor-associated factor (TRAF), preferably TRAF2, where inducing or agonizing the association up-regulates the cellular activity, and inhibiting or antagonizing the association down-regulates the cellular activity. INDEPENDENT CLAIMS are included for the following: (1) treating and/or preventing a condition of aberrant, unwanted or inappropriate cytokine-induced or tumor necrosis factor (TNF)-induced cellular activity in a mammal; (2) detecting an agent capable of modulating the interaction of TRAF with sphingosine kinase or its functional equivalent or derivative; (3) analyzing, designing and/or modifying an agent capable of interacting with the TRAF binding site of sphingosine kinase or its derivative and modulating at least one functional activity associated with the sphingosine kinase; (4) an agent described or identified in the methods cited above; and (5) a pharmaceutical condition comprising the modulatory agent described in the methods above, and one or more pharmaceutical carriers and/or diluents;

BIOTECHNOLOGY - Preferred Methods: The tumor necrosis factor (TNF)-induced cellular activity is the induction of anti-apoptotic characteristics, and modulation is down-regulation of the interaction of sphingosine kinase with TNF receptor-associated factor (TRAF). The TNF-induced cellular activity is the induction of pro-inflammatory, and the induction is down-regulation of the interaction of sphingosine kinase with TRAF. The agent binds, links or associates with the C-terminal region of sphingosine kinase, where the C-terminal region is the amino acid sequence of Pro-Pro-Glu Glu (I). The sphingosine kinase is preferably **human sphingosine kinase**, and the C-terminal region is the sequence of (I) at amino acid residue numbers 379-382 of a fully defined sequence of 384 amino acids (S1) given in the specification. Treating and/or preventing a condition of aberrant, unwanted or inappropriate cytokine-induced cellular activity in a mammal, comprises administering to the mammal an agent that modulates the interaction of sphingosine kinase with a TRAF, where inducing or agonizing the association up-regulates the cellular activity, and inhibiting or antagonizing the association down-regulates the cellular activity. Treating and/or preventing a condition of aberrant, unwanted or inappropriate TNF-induced cellular activity in a mammal, comprises administering to the mammal an agent that modulates the interaction of sphingosine kinase with a TRAF, preferably TRAF2, where inducing or agonizing the association up-regulates the cellular activity, and inhibiting or antagonizing the association down-regulates the cellular activity. The mammal is preferably human and the condition is a neoplastic condition. Detecting an agent capable of modulating the interaction of TRAF with sphingosine kinase or its functional equivalent or derivative, comprises contacting a cell or its extract containing the sphingosine kinase and TRAF or its functional equivalent or derivative

with a putative agent, and detecting an altered expression phenotype associated with the interaction. TRAF is preferably TRAF2. The altered expression phenotype is an altered apoptosis profile or is modulation of the functional activity of sphingosine kinase. Analyzing, designing and/or modifying an agent capable of interacting with the TRAF binding site of sphingosine kinase or its derivative and modulating at least one functional activity associated with the sphingosine kinase, comprises contacting the sphingosine kinase or its derivative with a putative agent and assessing the degree of interactive complementarity of the agent with the binding site. The TRAF binding site is the C-terminal region of sphingosine kinase, which is a **human sphingosine kinase**, and the C-terminal region is the sequence of (I) at amino acid residue numbers 379-382 of the sequence of S1.

ACTIVITY - Cytostatic; Antiinflammatory; Antirheumatic; Antiarthritic. No biological data given.

MECHANISM OF ACTION - Sphingosine Kinase Inhibitor; Sphingosine Kinase Stimulator; TRAF Agonist 2; TRAF Antagonist 2.

USE - The agent is useful for manufacturing a medicament for treating a mammal with a condition of aberrant, unwanted or inappropriate cytokine-induced or tumor necrosis factor (TNF)-induced cellular activity (claimed). The methods are useful for modulating cytokine-induced or TNF-induced cellular activity, or for treating or preventing a condition of aberrant, unwanted or inappropriate cytokine-induced or TNF-induced cellular activity in a mammal, such as neoplastic condition or inflammation (e.g. rheumatoid arthritis).

ADMINISTRATION - Dosage is about 0.1-1 mg/kg/day. Administration may be oral, intravenous, intraperitoneal, intramuscular, subcutaneous, intradermal, rectal, intratracheal, intracranial, intraocular, intrathecal, intracerebral, or intranasal.

EXAMPLE - Human embryonic kidney cell line 293T was transiently transfected with wild type TNF receptor-associated factor-2 (TRAF2), a dominant-negative TRAF2, or an empty vector. Over-expression of TRAF2 not only enhanced TNF-induced sphingosine kinase but also itself was capable of activating sphingosine kinase by two-fold compared with control transfectants. Immunoblotting assay showed equivalent expression levels of the transgenes in the presence or absence of TNF stimulation. (96 pages)

L4 ANSWER 33 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:276032 HCAPLUS
DOCUMENT NUMBER: 136:304111
TITLE: Regulation of **human sphingosine kinase**-like protein and uses in diagnosis, therapy and drug screening
INVENTOR(S): Kossida, Sophia; Encinas, Jeffrey
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028906	A2	20020411	WO 2001-EP11516	20011005
WO 2002028906	A3	20021114		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002023593	A5	20020415	AU 2002-23593	20011005
EP 1326986	A2	20030716	EP 2001-986303	20011005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004510429	T2	20040408	JP 2002-532488	20011005
PRIORITY APPLN. INFO.:			US 2000-238005P	P 20001006
			US 2001-314113P	P 20010823
			WO 2001-EP11516	W 20011005

AB Reagents which regulate **human sphingosine kinase**-like protein activity and reagents which bind to **human sphingosine kinase**-like protein gene products can be used to regulate intracellular signaling intracellular signaling and consequently cell proliferation and apoptosis. Such regulation is particularly useful for treating cancer, allergies including but not limited to asthma, autoimmune diseases such as rheumatoid arthritis, and central and peripheral nervous system disorders, such as Parkinson's disease.

L4 ANSWER 34 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2002:256587 HCAPLUS
DOCUMENT NUMBER:	136:291008
TITLE:	Methods and compositions for screening modulators of lipid kinases
INVENTOR(S):	Normant, Emmanuel; Melendez, Alirio; Casamitjana, Olivier; Moreau, Francois
PATENT ASSIGNEE(S):	Warner-Lambert Company, USA
SOURCE:	PCT Int. Appl., 44 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002027318	A1	20020404	WO 2001-EP11250	20010928
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1195604	A1	20020410	EP 2000-402684	20000929
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2423889	AA	20020404	CA 2001-2423889	20010928
AU 2001089939	A5	20020408	AU 2001-89939	20010928
EP 1195605	A1	20020410	EP 2001-402500	20010928
EP 1195605	B1	20040331		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002042091	A1	20020411	US 2001-964860	20010928
US 6723525	B2	20040420		
JP 2004509638	T2	20040402	JP 2002-530646	20010928
AT 263373	E	20040415	AT 2001-402500	20010928
PT 1195605	T	20040831	PT 2001-402500	20010928
ES 2218351	T3	20041116	ES 2001-1402500	20010928

PRIORITY APPLN. INFO.: EP 2000-402684 A 20000929
EP 2000-2000402684 A 20000929
WO 2001-EP11250 W 20010928

AB The present invention relates to methods of screening compds. that modulate lipid kinases activity. The invention is more preferably based on the SPA technol. to screen compds. that modulate the activity of lipid kinases, in particular membrane lipid kinases, more specifically sphingosine kinases. The invention also includes compns., products, kits, etc. for use in performing the above methods, as well as the compds. identified by said methods, and their uses.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 35 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:10690 HCAPLUS
DOCUMENT NUMBER: 136:81963
TITLE: Molecular variants of mammalian sphingosine kinase with reduced catalytic activity and therapeutic uses thereof
INVENTOR(S): Pitson, Stuart; Moretti, Paul; Zebol, Julia; Xia, Pu; Gamble, Jennifer; Vadas, Mathew; D'Andrea, Richard; Wattenberg, Binks
PATENT ASSIGNEE(S): Medvet Science Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000887	A1	20020103	WO 2001-AU730	20010620
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2414210	AA	20020103	CA 2001-2414210	20010620
AU 2001065699	A5	20020108	AU 2001-65699	20010620
EP 1299548	A1	20030409	EP 2001-942904	20010620
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004500903	T2	20040115	JP 2002-506202	20010620
BR 2001012059	A	20040727	BR 2001-12059	20010620
NZ 523343	A	20050324	NZ 2001-523343	20010620
NO 2002006265	A	20030224	NO 2002-6265	20021227
ZA 2003000214	A	20040408	ZA 2003-214	20030108

PRIORITY APPLN. INFO.: AU 2000-8408 A 20000628
AU 2000-8699 A 20000711
AU 2000-9980 A 20000908
AU 2001-2749 A 20010129
WO 2001-AU730 W 20010620

AB The present invention relates generally to a sphingosine kinase variant and to derivs., analogs, chemical equivalent and mimetics thereof exhibiting reduced catalytic activity and, more particularly, to sphingosine kinase variants which exhibit a reduced capacity to phosphorylate sphingosine to sphingosine-1-phosphate. The present invention also contemplates genetic sequences encoding said sphingosine kinase variants and derivs., analogs

and mimetics thereof. The variants of the present invention are useful in a range of therapeutic and prophylactic applications. Site-directed mutagenesis of a putative ATP-binding site (glycine in position 82 to aspartic acid, G82D) resulted in a catalytically inactive sphingosine kinase (SK) for phosphorylating sphingosine to sphingosine-1-phosphate. The G82D SK is expressed, as shown by Western blots, and does not suppress endogenous cellular SK activity. However, G82D SK decreases activation of sphingosine kinase activity after treatment of cells with agents such as TNF, IL-1, and PMA and it inhibits SK activity that is stimulated by the Ras oncogene. Another mutant G82A (glycine at position 82 substituted with alanine) retains about 5% of the wild-type level of catalytic activity. Anal. of substrate kinetics of G82A SK shows low affinity for ATP but wild-type affinity for sphingosine.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 36 OF 54 MEDLINE on STN DUPLICATE 6

ACCESSION NUMBER: 2002731982 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12393916
TITLE: The nucleotide-binding site of **human sphingosine kinase** 1.
AUTHOR: Pitson Stuart M; Moretti Paul A B; Zebol Julia R; Zareie Reza; Derian Claudia K; Darrow Andrew L; Qi Jenson; D'Andrea Richard J; Bagley Christopher J; Vadas Mathew A; Wattenberg Binks W
CORPORATE SOURCE: Hanson Institute, Division of Human Immunology, Institute of Medical and Veterinary Science, Frome Road, Adelaide SA 5000, Australia.. stuart.pitson@imvs.sa.gov.asu
SOURCE: Journal of biological chemistry, (2002 Dec 20) 277 (51) 49545-53. Electronic Publication: 2002-10-18. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20021227
Last Updated on STN: 20030214
Entered Medline: 20030212

AB Sphingosine kinase catalyzes the formation of sphingosine 1-phosphate, a lipid second messenger that has been implicated in a number of agonist-driven cellular responses including mitogenesis, anti-apoptosis, and expression of inflammatory molecules. Despite the importance of sphingosine kinase, very little is known regarding its structure or mechanism of catalysis. Moreover, sphingosine kinase does not contain recognizable catalytic or substrate-binding sites, based on sequence motifs found in other kinases. Here we have elucidated the nucleotide-binding site of **human sphingosine kinase** 1 (hSK1) through a combination of site-directed mutagenesis and affinity labeling with the ATP analogue, FSBA. We have shown that Gly(82) of hSK1 is involved in ATP binding since mutation of this residue to alanine resulted in an enzyme with an approximately 45-fold higher K(m)((ATP)). We have also shown that Lys(103) is important in catalysis since an alanine substitution of this residue ablates catalytic activity. Furthermore, we have shown that this residue is covalently modified by FSBA. Our data, combined with amino acid sequence comparison, suggest a motif of SGDGX(17-21)K is involved in nucleotide binding in the sphingosine kinases. This motif differs in primary sequence from all previously identified nucleotide-binding sites. It does, however, share some sequence and likely structural similarity with the highly conserved glycine-rich loop, which is known to be involved in anchoring and positioning the nucleotide in the catalytic site of many protein kinases.

L4 ANSWER 37 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:834308 HCAPLUS
DOCUMENT NUMBER: 138:117912
TITLE: Sphingosine kinase mediates vascular endothelial growth factor-induced activation of Ras and mitogen-activated protein kinases
AUTHOR(S): Shu, Xiaodong; Wu, Weicheng; Mosteller, Raymond D.; Broek, Daniel
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Norris Comprehensive Cancer Center, Keck School of Medicine at the University of Southern California, Los Angeles, CA, 90089, USA
SOURCE: Molecular and Cellular Biology (2002), 22(22), 7758-7768
CODEN: MCEBD4; ISSN: 0270-7306
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Vascular endothelial growth factor (VEGF) signaling is critical to the processes of angiogenesis and tumor growth. Here, evidence is presented for VEGF stimulation of sphingosine kinase (SPK) that affects not only endothelial cell signaling but also tumor cells expressing VEGF receptors. VEGF or phorbol 12-myristate 13-acetate treatment of the T24 bladder tumor cell line resulted in a time- and dose-dependent stimulation of SPK activity. In T24 cells, VEGF treatment reduced cellular sphingosine levels while raising that of sphingosine-1-phosphate. VEGF stimulation of T24 cells caused a slow and sustained accumulation of Ras-GTP and phosphorylated extracellular signal-regulated kinase (phospho-ERK) compared with that after EGF treatment. Small interfering RNA (siRNA) that targets SPK1, but not SPK2, blocks VEGF-induced accumulation of Ras-GTP and phospho-ERK in T24 cells. In contrast to EGF stimulation, VEGF stimulation of ERK1/2 phosphorylation was unaffected by dominant-neg. Ras-N17. Raf kinase inhibition blocked both VEGF- and EGF-stimulated accumulation of phospho-ERK1/2. Inhibition of SPK by pharmacol. inhibitors, a dominant-neg. SPK mutant, or siRNA that targets SPK blocked VEGF, but not EGF, induction of phospho-ERK1/2. We conclude that VEGF induces DNA synthesis in a pathway which sequentially involves protein kinase C (PKC), SPK, Ras, Raf, and ERK1/2. These data highlight a novel mechanism by which SPK mediates signaling from PKC to Ras in a manner independent of Ras-guanine nucleotide exchange factor.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 38 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:926610 HCAPLUS
DOCUMENT NUMBER: 138:23613
TITLE: Sphingosine kinase: a point of convergence in the action of diverse neutrophil priming agents
AUTHOR(S): MacKinnon, Alison C.; Buckley, Avril; Chilvers, Edwin R.; Rossi, Adriano G.; Haslett, Christopher; Sethi, Tariq
CORPORATE SOURCE: Lung Inflammatory Group, Center for Inflammation Research, University of Edinburgh, Edinburgh, EH8 9AG, UK
SOURCE: Journal of Immunology (2002), 169(11), 6394-6400
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Neutrophils are a vital component of the early acute inflammatory response, but can cause profound tissue damage when activated to excess or prevented from undergoing apoptosis. However, much remains unknown about the intracellular signaling pathways regulating neutrophil activity. The

structurally diverse neutrophil-priming agents platelet-activating factor, TNF-α, and the substance P analog [D-Arg6, D-Trp7,9,NmePhe8]-substance P(6-11) (SP-G) stimulated a rapid increase in sphingosine kinase activity in freshly isolated human neutrophils. This activity was blocked by preincubation with the sphingosine kinase inhibitor N,N-dimethylsphingosine (DMS). DMS also inhibited the increase in intracellular calcium concentration stimulated by platelet-activating factor, fMLP, and SP-G. This suggests that the increase in intracellular calcium concentration by these agents is dependent on sphingosine kinase activation and the generation of sphingosine-1-phosphate. Changes in cell polarization and the augmentation of the fMLP-induced superoxide anion generation, by all priming agents were also inhibited by DMS, while only the superoxide anion release was blocked by the phosphatidylinositol 3-kinase inhibitor LY294002. Moreover, SP-G and GM-CSF inhibited constitutive neutrophil apoptosis which was completely blocked by DMS. These results suggest a novel role for sphingosine kinase in the regulation of neutrophil priming.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT.

L4 ANSWER 39 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:644854 HCAPLUS
DOCUMENT NUMBER: 138:252780
TITLE: D-erythro-N,N-dimethylsphingosine inhibits bFGF-induced proliferation of cerebral, aortic, and coronary smooth muscle cells
AUTHOR(S): Xu, Cang-Bao; Zhang, Yaping; Stenman, Emelie; Edvinsson, Lars
CORPORATE SOURCE: Lund University, Department of Medicine, Division of Experimental Vascular Research, Lund, S-22185, Swed.
SOURCE: Atherosclerosis (Shannon, Ireland) (2002), 164(2), 237-243
CODEN: ATHSBL; ISSN: 0021-9150
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The role of sphingosine kinase (SphK) on basic fibroblast growth factor (bFGF)-induced proliferation of cerebral, aortic, and coronary smooth muscle cells (SMC) was addressed using D-erythro-N,N-dimethylsphingosine (DMS), an inhibitor of SphK which blocks conversion of sphingosine to sphingosine-1-phosphate (S1P). DMS concentration-dependently reduced the bFGF-induced proliferation of rat cerebral and aortic, and human coronary SMC. This suggests that SphK is 1 of the key enzymes in the mitogenic response to bFGF in vascular SMC as supported by the finding that S1P stimulated proliferation of SMC. Fumonisin B1, a dihydroceramidesynthase inhibitor which blocks the conversion of dihydrosphingosine to seramide, did not affect SMC proliferation induced by bFGF. Staurosporine, an inhibitor of protein kinase C (PKC), inhibited proliferation of SMC induced by bFGF, and both bFGF- and S1P-induced proliferation of SMC was sensitive to pertussis toxin (PTX), an inhibitor of Gi-protein activity. The present study thus demonstrates that SphK, PKC, and Gi-protein activities are required for bFGF-mitogenic signaling in SMC. The bFGF mitogenic effect in vascular SMC might at least in part act via the SphK pathway and a Gi-protein.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 40 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:857385 HCAPLUS
DOCUMENT NUMBER: 138:120688
TITLE: Sphingosine Kinase Type 1 Promotes Estrogen-Dependent Tumorigenesis of Breast Cancer MCF-7 Cells

AUTHOR(S): Nava, Victor E.; Hobson, John Peyton; Murthy, Shvetha; Milstien, Sheldon; Spiegel, Sarah
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC, 20007, USA
SOURCE: Experimental Cell Research (2002), 281(1), 115-127
CODEN: ECREAL; ISSN: 0014-4827
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The sphingolipid metabolite, sphingosine-1-phosphate (S1P), formed by phosphorylation of sphingosine, has been implicated in cell growth, suppression of apoptosis, and angiogenesis. In this study, we have examined the contribution of intracellular S1P to tumorigenesis of breast adenocarcinoma MCF-7 cells. Enforced expression of sphingosine kinase type 1 (SPHK1) increased S1P levels and blocked MCF-7 cell death induced by anti-cancer drugs, sphingosine, and TNF-α. SPHK1 also conferred a growth advantage, as determined by proliferation and growth in soft agar, which was estrogen dependent. While both ERK and Akt have been implicated in MCF-7 cell growth, SPHK1 stimulated ERK1/2 but had no effect on Akt. Surprisingly, parental growth of MCF-7 cells was only weakly stimulated by S1P or dihydro-S1P, ligands for the S1P receptors which usually mediate growth effects. When injected into mammary fat pads of ovariectomized nude mice implanted with estrogen pellets, MCF-7/SPHK1 cells formed more and larger tumors than vector transfectants with higher microvessel d. in their periphery. Collectively, our results suggest that SPHK1 may play an important role in breast cancer progression by regulating tumor cell growth and survival.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 41 OF 54 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 7
ACCESSION NUMBER: 2002:400436 BIOSIS
DOCUMENT NUMBER: PREV200200400436
TITLE: **Human sphingosine kinase** 1: Its localization and transcriptional control.
AUTHOR(S): Murate, T. [Reprint author]; Banno, Y.; Koizumi, K. T. [Reprint author]; Mori, N. [Reprint author]; Wada, A.; Igarashi, Y.; Takagi, A. [Reprint author]; Nozava, Y.
CORPORATE SOURCE: School of Health Sciences, Nagoya University, Nagoya, Japan
SOURCE: Experimental Hematology (Charlottesville), (June, 2002) Vol. 30, No. 6 Supplement 1, pp. 102. print.
Meeting Info.: 31st Annual Meeting of the International Society for Experimental Hematology. Montreal, Quebec, Canada. July 05-09, 2002.
CODEN: EXHMA6. ISSN: 0301-472X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jul 2002
Last Updated on STN: 24 Jul 2002

L4 ANSWER 42 OF 54 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2002228759 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11923095
TITLE: 1-O-Hexadecyl-2-desoxy-2-amino-sn-glycerol, a substrate for **human sphingosine kinase**.
AUTHOR: Gijsbers Sofie; Asselberghs Stanny; Herdewijn Piet; Van Veldhoven Paul P
CORPORATE SOURCE: Katholieke Universiteit Leuven, Faculteit Geneeskunde, Departement Moleculaire Celbiologie, Afdeling Farmakologie, Herestraat, Belgium.

SOURCE: Biochimica et biophysica acta, (2002 Jan 30) 1580 (1) 1-8.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020423
Last Updated on STN: 20020528
Entered Medline: 20020524

AB The substrate specificity of **human sphingosine kinase** was investigated using a bacterially expressed poly(His)-tagged protein. Only the D-erythro isomer of the sphingoid bases, sphinganine and sphingenine, was effectively phosphorylated. Long chain 1-alkanols, alkane-1,2-diols, 2-amino-1-alkanol or 1-amino-2-alkanol and short chain 2-amino-1,3-alkanediols were very poor substrates, indicating that the kinase is recognizing the chain length and the position of the amino and secondary hydroxy group. A free hydroxy group at carbon 3 is not a prerequisite, however, since 1-O-hexadecyl-2-desoxy-2-amino-sn-glycerol was an efficient substrate with an apparent K(m) value of 3.8 microM (versus 15.7 microM for sphingenine). This finding opens new perspectives to design sphingosine kinase inhibitors. It also calls for some caution since it cannot be excluded that this ether lipid analogue is formed from precursors that are frequently used in research on platelet activating factor or from phospholipid analogues which are less prone to degradation.

L4 ANSWER 43 OF 54 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
DUPLICATE 9
ACCESSION NUMBER: 2001-09987 BIOTECHDS
TITLE: New **human sphingosine-kinase** type-I gene for screening drug candidates particularly inhibitors used for preventing or treating e.g. atherosclerosis, thrombosis, asthma and diabetes; baculo virus vector, plasmid pcDNA3, plasmid pFastBacHTa, plasmid pFLAG or plasmid pCMV-mediated gene transfer, expression in host cell, antibody and DNA primer for drug screening
AUTHOR: Allen J; Gosink M; Melendez A J; Takacs L
PATENT ASSIGNEE: Warner
LOCATION: Morris Plains, NJ, USA.
PATENT INFO: WO 2001031029 3 May 2001
APPLICATION INFO: WO 2000-EP9498 27 Oct 2000
PRIORITY INFO: US 2000-180525 7 Feb 2000; US 1999-162307 28 Oct 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-300510 [31]

AB A purified or isolated DNA encoding a **human sphingosine -kinase** (hSK), which together with its encoded protein are applicable in drug screening particularly inhibitors for preventing or treating e.g. atherosclerosis, thrombosis, asthma and diabetes, is claimed. Also claimed are: a purified or isolated DNA encoding hSK protein having a specified sequence; a DNA having a specified 240 bp sequence; a recombinant vector containing the DNA; a recombinant host cell containing the DNA or the recombinant vector; an antisense oligonucleotide of the specified sequences; a transgenic animal (mouse) containing the DNA; a purified protein with the sequence of hSK; amplifying a DNA encoding hSK using a hSK-specific DNA primer; a kit for amplification containing the DNA primers and reagents for performing the amplification; producing a recombinant protein with a specified 384 amino acid sequence by culturing the recombinant host cell and recovering the protein from the culture; an antibody specific for the protein; and screening for drug candidates, particularly inhibitors of hSK. The

protein is useful in drug screening assays. (90pp)

L4 ANSWER 44 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:747808 HCAPLUS
DOCUMENT NUMBER: 135:300491
TITLE: Cloning, expression and therapeutic use of mammalian sphingosine kinase type 2 isoforms
INVENTOR(S): Spiegel, Sarah; Kohama, Takafumi
PATENT ASSIGNEE(S): Sankyo Company, Ltd., Japan; Georgetown University
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001074837	A1	20011011	WO 2001-US9664		20010326
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2404965	AA	20011011	CA 2001-2404965		20010326
US 2002042101	A1	20020411	US 2001-817676		20010326
US 6800470	B2	20041005			
EP 1268509	A1	20030102	EP 2001-924340		20010326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004500117	T2	20040108	JP 2001-572526		20010326
BR 2001009827	A	20040706	BR 2001-9827		20010326
NO 2002004727	A	20021203	NO 2002-4727		20021002
ZA 2002007930	A	20040127	ZA 2002-7930		20021002
US 2004203104	A1	20041014	US 2004-830677		20040422
PRIORITY APPLN. INFO.:			US 2000-194318P	P	20000403
			US 2001-817676	A	20010326
			WO 2001-US9664	W	20010326

AB The present invention concerns nucleic acids encoding mouse and **human sphingosine kinase** type 2 isoforms, methods for detecting agents or drugs which inhibit or promote sphingosine activity and therapeutic agents containing peptides or antibodies to peptides encoded by such nucleic acids. Amino acid and encoding cDNA sequences of the mouse and **human sphingosine kinase** type 2 isoforms are provided.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 45 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:618152 HCAPLUS
DOCUMENT NUMBER: 135:192176
TITLE: Cloning, sequence and therapeutic and diagnostic use of sphingosine kinases from human, rat and mouse
INVENTOR(S): Rastelli, Luca
PATENT ASSIGNEE(S): Curagen Corporation, USA; Genentech, Inc.
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060990	A2	20010823	WO 2001-US4789	20010214
WO 2001060990	A3	20020321		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2402148	AA	20010823	CA 2001-2402148	20010214
US 2002082203	A1	20020627	US 2001-784810	20010214
US 6858427	B2	20050222		
EP 1257637	A2	20021120	EP 2001-910701	20010214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2005123942	A1	20050609	US 2004-876281	20040624
PRIORITY APPLN. INFO.:			US 2000-182360P P	20000214
			US 2000-191261P P	20000322
			US 2001-784810 A3	20010214
			WO 2001-US4789 W	20010214

AB Amino acid and encoding cDNA sequences of two isoforms of **human sphingosine kinase** are disclosed. Amino acid and cDNA sequences of sphingosine kinases of rat and mouse are also provided. Also disclosed are antibodies that immunospecifically-bind to the sphingosine kinases, as well as derivs., variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.

L4 ANSWER 46 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:501714 HCAPLUS
DOCUMENT NUMBER: 135:224476
TITLE: Cell type-specific localization of sphingosine kinase 1a in human tissues
AUTHOR(S): Murate, Takashi; Banno, Yoshiko; Koizumi, Keiko T.; Watanabe, Kazuko; Mori, Naoyoshi; Wada, Atsushi; Igarashi, Yasuyuki; Takagi, Akira; Kojima, Tetsuhito; Asano, Haruhiko; Akao, Yukihiro; Yoshida, Shonen; Saito, Hidehiko; Nozawa, Yoshinori
CORPORATE SOURCE: Nagoya University School of Health Science, Nagoya, 461-8673, Japan
SOURCE: Journal of Histochemistry and Cytochemistry (2001), 49(7), 845-855
CODEN: JHCYAS; ISSN: 0022-1554
PUBLISHER: Histochemical Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cell type-specific localization of sphingosine kinase 1a (SPHK1a) in tissues was analyzed with a rabbit polyclonal antibody against the 16 C-terminal amino acids derived from the recently reported mouse cDNA sequence of SPHK1a. This antibody (anti-SPHK1a antibody) can react specifically with SPHK1a of mouse, rat, and human tissues. Utilizing its cross-reactivity to human SPHK1a, the cell-specific localization of SPHK1a

in human tissues was histochem. examined Strong pos. staining for SPHK1a was observed in the white matter in the cerebrum and cerebellum, the red nucleus and cerebral peduncle in the midbrain, the uraniferous tubules in the kidney, the endothelial cells in vessels of various organs, and in megakaryocytes and platelets. The lining cells of sinusoids in the liver and splenic cords in the spleen showed moderate staining. Columnar epithelia in the intestine and Leydig's cells in the testis showed weak staining patterns. In addition, TPA-treated HEL cells, a human leukemia cell line, showed a megakaryocytic phenotype accompanied with increases in immunostaining of both SPHK1a and SPHK enzyme activity, suggesting that SPHK1a may be a novel marker of megakaryocytic differentiation and that this antibody is also useful for in vitro study of differentiation models.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 47 OF 54 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:6948 SCISEARCH
THE GENUINE ARTICLE: 502RX
TITLE: Depolarisation induces rapid and transient formation of intracellular sphingosine-1-phosphate
AUTHOR: Alemany R; Kleuser B; Ruwisch L; Danneberg K; Lass H; Hashemi R; Spiegel S; Jakobs K H; Heringdorf D M Z (Reprint)
CORPORATE SOURCE: Univ Essen Gesamthsch Klinikum, Inst Pharmakol, Hufelandstr 55, D-45122 Essen, Germany (Reprint); Univ Essen Gesamthsch Klinikum, Inst Pharmakol, D-45122 Essen, Germany; Free Univ Berlin, Inst Pharm, D-14195 Berlin, Germany; Georgetown Univ, Med Ctr, Dept Biochem & Mol Biol, Washington, DC 20007 USA
COUNTRY OF AUTHOR: Germany; USA
SOURCE: FEBS LETTERS, (7 DEC 2001) Vol. 509, No. 2, pp. 239-244. Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. ISSN: 0014-5793.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 30
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Formation of sphingosine-1-phosphate (SPP) by sphingosine kinase serves as a signalling pathway for various membrane receptors. Here, we show that membrane depolarisation is another mechanism by which this pathway can be activated. Formation of [H-3]SPP as well as levels of endogenous SPP were rapidly and transiently increased in PC12 pheochromocytoma cells depolarised with high KCI. Time course and maximum were similar to those induced by bradykinin. Depolarisation-induced SPP production was also observed in RINm5F insulinoma cells, dependent on extracellular Ca2+ and fully suppressed by verapamil, thus apparently caused by Ca2+ influx via voltage-gated Ca2+ channels. Studies with sphingosine kinase inhibitors and overexpression of sphingosine kinase revealed a partial contribution of this pathway to depolarisation-induced noradrenaline release and Ca2+ increase. (C) 2001 Published by Elsevier Science B.V. on behalf of the Federation of European Biochemical Societies.

L4 ANSWER 48 OF 54 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2001700595 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11741582
TITLE: A point mutant of **human sphingosine kinase** 1 with increased catalytic activity.
AUTHOR: Pitson S M; Moretti P A; Zebol J R; Vadas M A; D'Andrea R J; Wattenberg B W
CORPORATE SOURCE: Hanson Centre for Cancer Research, Division of Human

Immunology, Institute of Medical and Veterinary Science,
Frome Road, Adelaide, SA 5000, Australia..
stuart.pitson@imvs.sa.gov.au
SOURCE: FEBS letters, (2001 Dec 7) 509 (2) 169-73.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011220
Last Updated on STN: 20020125
Entered Medline: 20020117
AB Sphingosine kinase (SK) catalyses the formation of sphingosine 1-phosphate, a lipid second messenger that has been implicated in mediating such fundamental biological processes as cell growth and survival. Very little is currently known regarding the structure or mechanisms of catalysis and activation of SK. Here we have tested the functional importance of Gly(113), a highly conserved residue of **human sphingosine kinase** 1 (hSK), by site-directed mutagenesis. Surprisingly, a Gly(113)-->Ala substitution generated a mutant that had 1.7-fold greater catalytic activity than wild-type hSK (hSK(WT)). Our data suggests that the Gly(113)-->Ala mutation increases catalytic efficiency of hSK, probably by inducing a conformational change that increases the efficiency of phosphoryl transfer. Interestingly, hSK(G113A) activity could be stimulated in HEK293T cells by cell agonists to a comparable extent to hSK(WT).

L4 ANSWER 49 OF 54 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
DUPLICATE 11
ACCESSION NUMBER: 2001-03254 BIOTECHDS
TITLE: Novel sphingosine-kinase protein and nucleic acid molecules for diagnosis, prophylaxis and treatment of rheumatoid arthritis, asthma, atherosclerosis, inflammation, meningitis, multiple sclerosis and septic shock;
involving vector plasmid pGEM4Z-mediated gene transfer for expression in Escherichia coli
AUTHOR: Pitson S M; Wattenberg B W; D'Andrea R J; Gamble J R; Vadas M A
PATENT ASSIGNEE: Johnson+Johnson
LOCATION: Everleigh, New South Wales, Australia.
PATENT INFO: WO 2000070028 23 Nov 2000
APPLICATION INFO: WO 2000-AU457 12 May 2000
PRIORITY INFO: AU 1999-1504 8 Jul 1999; AU 1999-339 13 May 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-016227 [02]
AB An isolated sphingosine-kinase protein (I) or its derivative, analog, chemical equivalent or mimetic, is new. Also claimed are: an isolated nucleic acid molecule (II) or its derivative or analog comprising a nucleotide sequence encoding or complementary to a sequence encoding (I); an agent for use in modulating sphingosine-kinase activity or expression; a pharmaceutical composition of (I) or the agent; an isolated antibody directed to (I) or (II); and diagnosing or monitoring a mammalian disease condition by screening for (I) in a biological sample isolated from the mammal. (I), (II) and the agent are useful for modulating expression, functional activity or cellular functional activity of sphingosine-kinase in a subject and also treating a mammal by modulating the activity of sphingosine-kinase. Diseases treated by regulating sphingosine-kinase cellular activity include rheumatoid arthritis, asthma, atherosclerosis, inflammation, meningitis, multiple sclerosis and septic shock. Recombinant **human sphingosine-kinase** was expressed by transforming the vector plasmid pGEM4Z into Escherichia coli

BL21. (100pp)

L4 ANSWER 50 OF 54 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
DUPLICATE 12
ACCESSION NUMBER: 2000-14580 BIOTECHDS
TITLE: New **human sphingosine-kinase**-A, -B and -C polynucleotides and polypeptides useful in e.g. chromosome and gene mapping, and detecting inflammation or disease associated with abnormal levels of sphingosine-kinase expression;
vector-mediated gene transfer, expression in host cell, recombinant protein production, agonist, antagonist, antisense and DNA probe for disease therapy, diagnosis and gene therapy
AUTHOR: Munroe D; Gupta A; Falzone G R
PATENT ASSIGNEE: NPS-Allelix
LOCATION: Mississauga, Ontario, Canada.
PATENT INFO: WO 2000052173 8 Sep 2000
APPLICATION INFO: WO 2000-CA223 2 Mar 2000
PRIORITY INFO: US 990122516 2 Mar 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2000-572185 [53]
AB An isolated DNA (I) encoding **human sphingosine-kinase** (hSK)-A, -B and -C or their variants, is claimed. Also claimed are: an isolated DNA sequence complementary to (I); a composition with (I) and an excipient; a vector with (I); a host cell with the above vector; making a purified protein with the protein sequence for hSK by culturing the host cell and recovering the protein; a purified protein produced by the above method; and screening a compound for its antagonistic or agonistic properties against hSK activity by contacting the host cell with the compound and measuring the inhibition or activation of hSK activity. The hSK DNAs may be used as hybridization DNA probes, in the construction of oligomers for polymerase chain reaction, for chromosome gene mapping, in the recombinant production of hSK-A, -B and -C, and in the generation of antisense DNA or RNA. The DNA sequence for hSK can be used to detect inflammation or disease associated with abnormal levels of SK expression, or to detect differences in gene sequence between normal and carrier or affected individuals. (81pp)

L4 ANSWER 51 OF 54 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 2000387082 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10751414
TITLE: Molecular cloning and functional characterization of a novel mammalian sphingosine kinase type 2 isoform.
AUTHOR: Liu H; Sugiura M; Nava V E; Edsall L C; Kono K; Poulton S; Milstien S; Kohama T; Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, D. C. 20007, USA.
CONTRACT NUMBER: GM43880 (NIGMS)
SOURCE: Journal of biological chemistry, (2000 Jun 30) 275 (26) 19513-20.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF245447; GENBANK-AF245448
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000818
Last Updated on STN: 20000818
Entered Medline: 20000810

AB Sphingosine-1-phosphate (SPP) has diverse biological functions acting inside cells as a second messenger to regulate proliferation and survival, and extracellularly, as a ligand for G protein-coupled receptors of the endothelial differentiation gene-1 subfamily. Based on sequence homology to murine and **human sphingosine kinase**-1 (SPHK1), which we recently cloned (Kohama, T., Oliver, A., Edsall, L. , Nagiec, M. M., Dickson, R., and Spiegel, S. (1998) J. Biol. Chemical 273, 23722-23728), we have now cloned a second type of mouse and **human sphingosine kinase** (mSPHK2 and hSPHK2). mSPHK2 and hSPHK2 encode proteins of 617 and 618 amino acids, respectively, both much larger than SPHK1, and though diverging considerably, both contain the conserved domains found in all SPHK1s. Northern blot analysis revealed that SPHK2 mRNA expression had a strikingly different tissue distribution from that of SPHK1 and appeared later in embryonic development. Expression of SPHK2 in HEK 293 cells resulted in elevated SPP levels. d-erythro-dihydrosphingosine was a better substrate than d-erythro-sphingosine for SPHK2. Surprisingly, d, l-threo-dihydrosphingosine was also phosphorylated by SPHK2. In contrast to the inhibitory effects on SPHK1, high salt concentrations markedly stimulated SPHK2. Triton X-100 inhibited SPHK2 and stimulated SPHK1, whereas phosphatidylserine stimulated both type 1 and type 2 SPHK. Thus, SPHK2 is another member of a growing class of sphingolipid kinases that may have novel functions.

L4 ANSWER 52 OF 54 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 2001097784 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10947957
TITLE: **Human sphingosine kinase**: purification, molecular cloning and characterization of the native and recombinant enzymes.
AUTHOR: Pitson S M; D'andrea R J; Vandeleur L; Moretti P A; Xia P; Gamble J R; Vadas M A; Wattenberg B W
CORPORATE SOURCE: Hanson Centre for Cancer Research, Division of Human Immunology, Institute of Medical and Veterinary Science, Frome Road, Adelaide 5000, SA, Australia.
SOURCE: Biochemical journal, (2000 Sep 1) 350 Pt 2 429-41. Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF200328
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201

AB Sphingosine 1-phosphate (S1P) is a novel lipid messenger that has important roles in a wide variety of mammalian cellular processes including growth, differentiation and death. Basal levels of S1P in mammalian cells are generally low, but can increase rapidly and transiently when cells are exposed to mitogenic agents and other stimuli. This increase is largely due to increased activity of sphingosine kinase (SK), the enzyme that catalyses its formation. In the current study we have purified, cloned and characterized the first human SK to obtain a better understanding of its biochemical activity and possible activation mechanisms. The enzyme was purified to homogeneity from human placenta using ammonium sulphate precipitation, anion-exchange chromatography, calmodulin-affinity chromatography and gel-filtration chromatography. This resulted in a purification of over 10(6)-fold from the original placenta extract. The enzyme was cloned and expressed in active form in both HEK-293T cells and Escherichia coli, and the recombinant E. coli-derived SK purified to homogeneity. To establish whether post-translational modifications lead to activation of human SK activity

we characterized both the purified placental enzyme and the purified recombinant SK produced in E. coli, where such modifications would not occur. The premise for this study was that post-translational modifications are likely to cause conformational changes in the structure of SK, which may result in detectable changes in the physico-chemical or catalytic properties of the enzyme. Thus the enzymes were characterized with respect to substrate specificity and kinetics, inhibition kinetics and various other physico-chemical properties. In all cases, both the native and recombinant SKs displayed remarkably similar properties, indicating that post-translational modifications are not required for basal activity of human SK.

L4 ANSWER 53 OF 54 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 2000263733 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10802064
TITLE: Functional characterization of **human sphingosine kinase**-1.
AUTHOR: Nava V E; Lacana E; Poulton S; Liu H; Sugiura M; Kono K; Milstien S; Kohama T; Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, 353 Basic Science Building, 3900 Reservoir Road NW, Washington, DC 20007, USA.
CONTRACT NUMBER: GM43880 (NIGMS)
SOURCE: FEBS letters, (2000 May 4) 473 (1) 81-4.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF238083
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000616
Last Updated on STN: 20000616
Entered Medline: 20000605

AB Sphingosine kinase catalyzes the phosphorylation of sphingosine to form sphingosine 1-phosphate (SPP), a novel lipid mediator with both intra- and extracellular functions. Based on sequence identity to murine sphingosine kinase (mSPHK1a), we cloned and characterized the first **human sphingosine kinase** (hSPHK1). The open reading frame of hSPHK1 encodes a 384 amino acid protein with 85% identity and 92% similarity to mSPHK1a at the amino acid level. Similar to mSPHK1a, when HEK293 cells were transfected with hSPHK1, there were marked increases in sphingosine kinase activity resulting in elevated SPP levels. hSPHK1 also specifically phosphorylated D-erythro-sphingosine and to a lesser extent sphinganine, but not other lipids, such as D,L-threo-dihydrosphingosine, N, N-dimethylsphingosine, diacylglycerol, ceramide, or phosphatidylinositol. Northern analysis revealed that hSPHK1 was widely expressed with highest levels in adult liver, kidney, heart and skeletal muscle. Thus, hSPHK1 belongs to a highly conserved unique lipid kinase family that regulates diverse biological functions.

L4 ANSWER 54 OF 54 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 2000323213 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10863092
TITLE: **Human sphingosine kinase**: molecular cloning, functional characterization and tissue distribution.
AUTHOR: Melendez A J; Carlos-Dias E; Gosink M; Allen J M; Takacs L
CORPORATE SOURCE: Department of Molecular and Cellular Biology, Institut de Recherche Jouveinal/Parke-Davis, Fresnes, France.. alirio.melendez@wl.com
SOURCE: Gene, (2000 Jun 13) 251 (1) 19-26.

Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000810
Last Updated on STN: 20000810
Entered Medline: 20000727

AB Sphingosine-1-phosphate (SPP), the product of sphingosine kinase, is an important signaling molecule with intra- and extracellular functions. The cDNA for the mouse sphingosine kinase has recently been reported. In this paper we describe the cloning, expression and characterization of the **human sphingosine kinase** (huSPHK1). Sequence analysis comparison revealed that this kinase is evolutionarily very conserved, having a high degree of homology with the murine enzyme, and presenting several conserved regions with bacteria, yeast, plant, and mammalian proteins. Expressed huSPHK1 cDNA specifically phosphorylates D-erythro-sphingosine and, to a lesser extent, D, L-erythro-dihydrosphingosine, and not at all the 'threo' isoforms of dihydrosphingosine; hydroxy-ceramide or non-hydroxy-ceramide; diacylglycerol (DAG); phosphatidylinositol (PI); phosphatidylinositol-4-phosphate (PIP); or phosphatidylinositol-4, 5-bisphosphate (PIP(2)). huSPHK1 shows typical Michaelis-Menten kinetics (V(max)=56microM and K(m)=5microM). The kinase is inhibited by D,L-threo-dihydrosphingosine (K(i)=3microM), and by N, N-dimethyl-sphingosine (K(i)=5microM). Northern blots indicate highest expression in adult lung and spleen, followed by peripheral blood leukocyte, thymus and kidney, respectively. It is also expressed in brain and heart. In addition, database searches with the stSG2854 sequence indicate that huSPHK1 is also expressed in endothelial cells, retinal pigment epithelium, and senescent fibroblasts.

=> d his

(FILE 'HOME' ENTERED AT 10:16:41 ON 23 JUN 2005)

FILE 'STNGUIDE' ENTERED AT 10:16:54 ON 23 JUN 2005

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 10:17:40 ON 23 JUN 2005

L1 22912 S SPHINGOSINE
L2 1950 S L1 (W)KINASE?
L3 104 S HUMAN (W)L2
L4 54 DUP REM L3 (50 DUPLICATES REMOVED)

=> s clon? or express? or recombinant
5 FILES SEARCHED...
L5 7132348 CLON? OR EXPRESS? OR RECOMBINANT

=> s l4 and l5
L6 36 L4 AND L5

=> s mimetic? or derivative? or analogue?
L7 3507345 MIMETIC? OR DERIVATIVE? OR ANALOGUE?

=> s l2 and l7
L8 388 L2 AND L7

=> s sphingosine-1-phosphate
L9 6947 SPHINGOSINE-1-PHOSPHATE

=> s l8 and l9

L10 320 L8 AND L9

=> s l10 and kinase?
L11 320 L10 AND KINASE?

=> dup rem l11
PROCESSING COMPLETED FOR L11
L12 211 DUP REM L11 (109 DUPLICATES REMOVED)

=> s human and l12
L13 126 HUMAN AND L12

=> d 1-126 ibib

L13 ANSWER 1 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2005243363 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15881612
TITLE: **Sphingosine 1-phosphate** is involved in cytoprotective actions of calcitriol in **human** fibroblasts and enhances the intracellular Bcl-2/Bax rheostat.
AUTHOR: Sauer B; Gonska H; Manggau M; Kim D S; Schraut C; Schafer-Korting M; Kleuser B
CORPORATE SOURCE: Institut fur Pharmazie, Freie Universitat Berlin, Germany.
SOURCE: Die Pharmazie, (2005 Apr) 60 (4) 298-304. Journal code: 9800766. ISSN: 0031-7144.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200505
ENTRY DATE: Entered STN: 20050511
Last Updated on STN: 20050601
Entered Medline: 20050531

L13 ANSWER 2 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2005225230 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15802614
TITLE: Immunomodulator FTY720 Induces eNOS-dependent arterial vasodilatation via the lysophospholipid receptor S1P3.
AUTHOR: Tolle Markus; Levkau Bodo; Keul Petra; Brinkmann Volker; Giebing Gunter; Schonfelder Gilbert; Schafers Michael; von Wnuck Lipinski Karin; Jankowski Joachim; Jankowski Vera; Chun Jerold; Zidek Walter; Van der Giet Markus
CORPORATE SOURCE: Med. Klinik IV, Charite-Campus Benjamin Franklin, Berlin, Germany.
SOURCE: Circulation research, (2005 Apr 29) 96 (8) 913-20. Electronic Publication: 2005-03-31. Journal code: 0047103. ISSN: 1524-4571.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20050430
Last Updated on STN: 20050430

L13 ANSWER 3 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2005046571 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15522918
TITLE: Lysophosphatidic acid triggers calcium entry through a non-store-operated pathway in **human** neutrophils.
AUTHOR: Itagaki Kiyoshi; Kannan Kolenkode B; Hauser Carl J
CORPORATE SOURCE: The Department of Surgery, Division of Trauma, University

of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark , NJ 07103, USA.. itagakki@umdnj.edu
CONTRACT NUMBER: GM-50179 (NIGMS)
SOURCE: Journal of leukocyte biology, (2005 Feb) 77 (2) 181-9. Electronic Publication: 2004-11-02. Journal code: 8405628. ISSN: 0741-5400.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 20050128
Last Updated on STN: 20050316
Entered Medline: 20050315

L13 ANSWER 4 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2005016608 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15643073
TITLE: **Sphingosine kinase** regulates the sensitivity of Dictyostelium discoideum cells to the anticancer drug cisplatin.
AUTHOR: Min Junxia; Traynor David; Stegner Andrew L; Zhang Lei; Hanigan Marie H; Alexander Hannah; Alexander Stephen
CORPORATE SOURCE: Division of Biological Sciences, University of Missouri, Columbia, MO 65211-7400, USA.
CONTRACT NUMBER: CA57530 (NCI)
CA95872 (NCI)
GM53929 (NIGMS)
SOURCE: Eukaryotic cell, (2005 Jan) 4 (1) 178-89. Journal code: 101130731. ISSN: 1535-9778.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200505
ENTRY DATE: Entered STN: 20050112
Last Updated on STN: 20050525
Entered Medline: 20050524

L13 ANSWER 5 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2005000830 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15485866
TITLE: **Sphingosine kinase** 1 (SPHK1) is induced by transforming growth factor-beta and mediates TIMP-1 up-regulation.
AUTHOR: Yamanaka Masayoshi; Shegogue Daniel; Pei Heuping; Bu Shizhong; Bielawska Alicja; Bielawski Jacek; Pettus Benjamin; Hannun Yusuf A; Obeid Lina; Trojanowska Maria
CORPORATE SOURCE: Division of Rheumatology and Immunology, Medical University of South Carolina, Charleston, SC 29725, USA.
CONTRACT NUMBER: AG16538 (NIA)
GM43825 (NIGMS)
P60 AR049459 (NIAMS)
SOURCE: Journal of biological chemistry, (2004 Dec 24) 279 (52) 53994-4001. Electronic Publication: 2004-10-12. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 20050104
Last Updated on STN: 20050315

Entered Medline: 20050314

L13 ANSWER 6 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004620045 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15580017
TITLE: Attenuation of shock-induced acute lung injury by **sphingosine kinase** inhibition.
AUTHOR: Lee Cindy; Xu Da-Zhong; Feketeova Eleonora; Kannan K B; Yun Jong K; Deitch Edwin A; Fekete Zoltan; Livingston David H; Hauser Carl J
CORPORATE SOURCE: Department of Surgery, Division of Trauma,, University of Medicine and Dentistry of New Jersey Medical School, Newark, New Jersey, USA.
CONTRACT NUMBER: GM-59179 (NIGMS)
SOURCE: Journal of trauma, (2004 Nov) 57 (5) 955-60.
Journal code: 0376373. ISSN: 0022-5282.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 20041220
Last Updated on STN: 20050216
Entered Medline: 20050214

L13 ANSWER 7 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004596801 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15570180
TITLE: Overview of FTY720 clinical pharmacokinetics and pharmacology.
AUTHOR: Kovarik John M; Schmouder Robert L; Slade Alan J
CORPORATE SOURCE: Novartis Pharmaceuticals, Basel, Switzerland..
john.kovarik@pharma.novartis.com
SOURCE: Therapeutic drug monitoring, (2004 Dec) 26 (6) 585-7. Ref: 17
Journal code: 7909660. ISSN: 0163-4356.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 20041201
Last Updated on STN: 20050325
Entered Medline: 20050324

L13 ANSWER 8 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004528417 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15498114
TITLE: mitochondrial ceramidase overexpression up-regulates Bcl-2 protein level in K562 cells, probably through its metabolite **sphingosine-1-phosphate**.
AUTHOR: Wang Fu-Xu; Dong Zuo-Ren; Liu Ze-Lin; Pan Ling; Luo Jian-Min; Zhang Xue-Jun; Hao Hong-Ling; Li Xiao-Ling; Yang Jing-Ci; Jiang Ling-Ling
CORPORATE SOURCE: Department of Hematology, The Second Hospital of Hebei Medical University, Shijiazhuang 050000, China..
wangfx@hebmu.edu.cn
SOURCE: Zhongguo shi yan xue ye xue za zhi / Zhongguo bing li sheng li xue hui = Journal of experimental hematology / Chinese Association of Pathophysiology, (2004 Oct) 12 (5) 577-83.

Journal code: 101084424. ISSN: 1009-2137.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 20041023
Last Updated on STN: 20050127
Entered Medline: 20050126

L13 ANSWER 9 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004518413 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15302883
TITLE: Anaphylatoxin signaling in **human** neutrophils. A key role for **sphingosine kinase**.
AUTHOR: Ibrahim Farazeela Bte Mohd; Pang See Jay; Melendez Alirio J
CORPORATE SOURCE: Department of Physiology, National University of Singapore, Singapore 117597.
SOURCE: Journal of biological chemistry, (2004 Oct 22) 279 (43) 44802-11. Electronic Publication: 2004-08-09.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 20041019
Last Updated on STN: 20041220
Entered Medline: 20041214

L13 ANSWER 10 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004428013 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15334188
TITLE: Vascular **sphingosine-1-phosphate** S1P1 and S1P3 receptors.
AUTHOR: Waeber Christian; Blondeau Nicolas; Salomone Salvatore
CORPORATE SOURCE: Department of Radiology, Massachusetts General Hospital, Charlestown, Massachusetts 02129, USA. waeber@helix.mgh.harvard.edu.
CONTRACT NUMBER: NS043216 (NINDS)
SOURCE: Drug news & perspectives, (2004 Jul-Aug) 17 (6) 365-82.
Ref: 207
Journal code: 8809164. ISSN: 0214-0934.
PUB. COUNTRY: Spain
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 20040831
Last Updated on STN: 20041221
Entered Medline: 20041220

L13 ANSWER 11 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004413018 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15193146
TITLE: Delta-catenin/NPRAP (neural plakophilin-related armadillo repeat protein) interacts with and activates **sphingosine kinase** 1.
AUTHOR: Fujita Toshitada; Okada Taro; Hayashi Shun; Jahangeer Saleem; Miwa Noriko; Nakamura Shun-ichi
CORPORATE SOURCE: Division of Biochemistry, Department of Molecular and Cellular Biology, Kobe University Graduate School of

Medicine, Kobe 650-0017, Japan.
SOURCE: Biochemical journal, (2004 Sep 1) 382 (Pt 2) 717-23.
Journal code: 2984726R. ISSN: 1470-8728.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 20040820
Last Updated on STN: 20050223
Entered Medline: 20050222

L13 ANSWER 12 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004381674 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15208267
TITLE: The immune modulator FTY720 targets **sphingosine-kinase**-dependent migration of **human** monocytes in response to amyloid beta-protein and its precursor.
AUTHOR: Kaneider Nicole C; Lindner Julia; Feistritzer Clemens; Sturn Daniel H; Mosheimer Birgit A; Djanani Angela M; Wiedermann Christian J
CORPORATE SOURCE: Division of General Internal Medicine, Department of Internal Medicine, Innsbruck University Hospital, Innsbruck, Austria.
SOURCE: FASEB journal : official publication of the Federation of American Societies for Experimental Biology, (2004 Aug) 18 (11) 1309-11. Electronic Publication: 2004-06-18.
Journal code: 8804484. ISSN: 1530-6860.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 20040803
Last Updated on STN: 20050209
Entered Medline: 20050208

L13 ANSWER 13 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004362606 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15265887
TITLE: Antisense knockdown of **sphingosine kinase** 1 in **human** macrophages inhibits C5a receptor-dependent signal transduction, Ca2+ signals, enzyme release, cytokine production, and chemotaxis.
AUTHOR: Melendez Alirio J; Ibrahim Farazeela Bte Mohd
CORPORATE SOURCE: Department of Physiology, National University of Singapore, Singapore.. phsmraj@nus.edu.sg
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2004 Aug 1) 173 (3) 1596-603.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 20040722
Last Updated on STN: 20041103
Entered Medline: 20041102

L13 ANSWER 14 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004362326 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15265705

TITLE: **Sphingosine kinase** activation regulates hepatocyte growth factor induced migration of endothelial cells.
AUTHOR: Duan Hai-Feng; Wu Chu-Tse; Lu Ying; Wang Hua; Liu Hong-Jun; Zhang Qun-Wei; Jia Xiang-Xu; Lu Zhu-Zhuang; Wang Li-Sheng
CORPORATE SOURCE: Department of Experimental Hematology, Beijing Institute of Radiation Medicine, Beijing 100850, People's Republic of China.
SOURCE: Experimental cell research, (2004 Aug 15) 298 (2) 593-601. Journal code: 0373226. ISSN: 0014-4827.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 20040722
Last Updated on STN: 20041005
Entered Medline: 20041004

L13 ANSWER 15 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004355360 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15258895
TITLE: Mechanisms of cardioprotection by lysophospholipids.
AUTHOR: Karliner Joel S
CORPORATE SOURCE: Cardiology Section, VA Medical Center, Department of Medicine and Cardiovascular Research Institute, University of California, San Francisco, California 94121, USA.. Joel.Karlinger@med.va.gov
CONTRACT NUMBER: 1PO1 HL 068738 (NHLBI)
SOURCE: Journal of cellular biochemistry, (2004 Aug 15) 92 (6) 1095-103. Ref: 45
Journal code: 8205768. ISSN: 0730-2312.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 20040720
Last Updated on STN: 20050319
Entered Medline: 20050318

L13 ANSWER 16 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004340410 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15242760
TITLE: Prosaposin: a new player in cell death prevention of U937 monocytic cells.
AUTHOR: Misasi Roberta; Garofalo Tina; Di Marzio Luisa; Mattei Vincenzo; Gizzi Chiara; Hiraiwa Masao; Pavan Antonio; Grazia Cifone Maria; Sorice Maurizio
CORPORATE SOURCE: Dipartimento di Medicina Sperimentale e Patologia, Universita La Sapienza, Roma, Rome, Italy.. roberta.misasi@uniroma1.it
SOURCE: Experimental cell research, (2004 Aug 1) 298 (1) 38-47. Journal code: 0373226. ISSN: 0014-4827.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 20040710
Last Updated on STN: 20040909

Entered Medline: 20040908

L13 ANSWER 17 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004307764 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15210056
TITLE: Sphingosine signaling and atherogenesis.
AUTHOR: Xu Cang-bao; Hansen-Schwartz Jacob; Edvinsson Lars
CORPORATE SOURCE: Division of Experimental Vascular Research, Institute of Medicine, Lund University, Sweden.. Cang-Bao.Xu@med.lu.se
SOURCE: Acta pharmacologica Sinica, (2004 Jul) 25 (7) 849-54. Ref: 34
Journal code: 100956087. ISSN: 1671-4083.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040624
Last Updated on STN: 20040901
Entered Medline: 20040831

L13 ANSWER 18 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004266676 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15165029
TITLE: Functional characterization of **sphingosine 1-phosphate** receptor agonist in **human** endothelial cells.
AUTHOR: Butler Jeannene; Lana Diana; Round Oliver; LaMontagne Kenneth
CORPORATE SOURCE: Novartis Institute for Biomedical Research, Inc., One Health Plaza, Room 2223, Bldg 436, East Hanover, NJ 07936, USA.
SOURCE: Prostaglandins & other lipid mediators, (2004 Jan) 73 (1-2) 29-45.
Journal code: 9808648. ISSN: 1098-8823.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 20040529
Last Updated on STN: 20050210
Entered Medline: 20050209

L13 ANSWER 19 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004256346 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14742298
TITLE: **Sphingosine kinase** mediates activation of extracellular signal-related **kinase** and Akt by respiratory syncytial virus.
AUTHOR: Monick Martha M; Cameron Kelli; Powers Linda S; Butler Noah S; McCoy Diann; Mallampalli Rama K; Hunninghake Gary W
CORPORATE SOURCE: Division of Pulmonary, Critical Care, and Occupational Medicine, Room 100, EMRB, University of Iowa Roy J. and Lucille A. Carver College of Medicine, Iowa City, IA 52242, USA.. martha-monick@uiowa.edu
CONTRACT NUMBER: ES-09607 (NIEHS)
HL 68135 (NHLBI)
HL-55584 (NHLBI)
HL-60316 (NHLBI)
RR00059 (NCRR)

SOURCE: American journal of respiratory cell and molecular biology, (2004 Jun) 30 (6) 844-52. Electronic Publication: 2004-01-23.
Journal code: 8917225. ISSN: 1044-1549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20040525
Last Updated on STN: 20040630
Entered Medline: 20040629

L13 ANSWER 20 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004197284 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15095287
TITLE: Intraocular gutless adenoviral-vectored VEGF stimulates anterior segment but not retinal neovascularization.
AUTHOR: Oshima Yuji; Takahashi Kyoichi; Oshima Sachiko; Saishin Yoshitsugu; Saishin Yumiko; Silva Raquel Lima; Liang Xaoling; Reddy P Seshidhar; Ganesh Shanthi; Brann Terrence; Liau Gene; Kaleko Michael; Connelly Sheila; Campochiaro Peter A
CORPORATE SOURCE: Department of Ophthalmology, The Johns Hopkins University School of Medicine, Maumenee, Baltimore, Maryland 21287, USA.
CONTRACT NUMBER: EY05951 (NEI)
EY12609 (NEI)
P30EY1765 (NEI)
SOURCE: Journal of cellular physiology, (2004 Jun) 199 (3) 399-411.
Journal code: 0050222. ISSN: 0021-9541.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20040420
Last Updated on STN: 20040618
Entered Medline: 20040617

L13 ANSWER 21 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004165949 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15059942
TITLE: Point-counterpoint of **sphingosine 1-phosphate** metabolism.
AUTHOR: Saba Julie D; Hla Timothy
CORPORATE SOURCE: Children's Hospital of Oakland Research Institute, Oakland, Calif, USA.
CONTRACT NUMBER: CA77528 (NCI)
GM66954 (NIGMS)
HL67330 (NHLBI)
HL70694 (NHLBI)
SOURCE: Circulation research, (2004 Apr 2) 94 (6) 724-34. Ref: 113
Journal code: 0047103. ISSN: 1524-4571.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20040403
Last Updated on STN: 20040717
Entered Medline: 20040716

L13 ANSWER 22 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004100766 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14991774
TITLE: Glucocorticoids mediate differential anti-apoptotic effects in **human** fibroblasts and keratinocytes via **sphingosine-1-phosphate** formation.
AUTHOR: Hammer S; Sauer B; Spika I; Schraut C; Kleuser B; Schafer-Korting M
CORPORATE SOURCE: Institut fur Pharmazie, Abteilung fur Pharmakologie und Toxikologie, Freie Universitat Berlin, Berlin, Germany.
SOURCE: Journal of cellular biochemistry, (2004 Mar 1) 91 (4) 840-51.
Journal code: 8205768. ISSN: 0730-2312.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 20040302
Last Updated on STN: 20041220
Entered Medline: 20041210

L13 ANSWER 23 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004095066 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14984734
TITLE: Identification of PECAM-1 association with **sphingosine kinase** 1 and its regulation by agonist-induced phosphorylation.
AUTHOR: Fukuda Yu; Aoyama Yuki; Wada Atsushi; Igarashi Yasuyuki
CORPORATE SOURCE: Department of Biomembrane and Biofunctional Chemistry, Graduate School of Pharmaceutical Sciences, Hokkaido University, Kita 12, Nishi 6, Kita, Sapporo 60-0812, Japan.
SOURCE: Biochimica et biophysica acta, (2004 Feb 27) 1636 (1) 12-21.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040302
Last Updated on STN: 20040806
Entered Medline: 20040805

L13 ANSWER 24 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004067788 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14769343
TITLE: Fluorescence-based assay of **sphingosine kinases**.
AUTHOR: Billich Andreas; Ettmayer Peter
CORPORATE SOURCE: Novartis Research Institute Vienna, Brunner Strasse 59, A-1235 Vienna, Austria.. andreas.billich@pharma.novartis.com
SOURCE: Analytical biochemistry, (2004 Mar 1) 326 (1) 114-9.
Journal code: 0370535. ISSN: 0003-2697.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 20040211

Last Updated on STN: 20040915
Entered Medline: 20040914

L13 ANSWER 25 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2004005277 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14703013
TITLE: Platelets induce reactive oxygen species-dependent growth of **human** skin fibroblasts.
AUTHOR: Berg Cecilia; Trofast Catarina; Bengtsson Torbjorn
CORPORATE SOURCE: Division of Medical Microbiology, Department of Molecular and Clinical Medicine, Faculty of Health Sciences, Linkoping University, Linkoping, Sweden.. cecbe@ifm.liu.se
SOURCE: European journal of cell biology, (2003 Nov) 82 (11) 565-71.
Journal code: 7906240. ISSN: 0171-9335.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20040106
Last Updated on STN: 20040722
Entered Medline: 20040721

L13 ANSWER 26 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2003601624 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14685698
TITLE: **Sphingosine 1-phosphate** signal survival and mitogenesis are mediated by lipid-stereospecific binding of triacylglycerol-rich lipoproteins.
AUTHOR: Pacheco Y M; Abia R; Olivera A; Spiegel S; Ruiz-Gutierrez V; Muriana F J G
CORPORATE SOURCE: Instituto de la Grasa, CSIC, 41012 Seville, Spain.
SOURCE: Cellular and molecular life sciences : CMLS, (2003 Dec) 60 (12) 2757-66.
Journal code: 9705402. ISSN: 1420-682X.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20031220
Last Updated on STN: 20040212
Entered Medline: 20040211

L13 ANSWER 27 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2003544249 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14623109
TITLE: Photolysis of intracellular caged **sphingosine-1-phosphate** causes Ca2+ mobilization independently of G-protein-coupled receptors.
AUTHOR: Meyer zu Heringdorf Dagmar; Liliom Karoly; Schaefer Michael; Danneberg Kerstin; Jaggar Jonathan H; Tigyi Gabor; Jakobs Karl H
CORPORATE SOURCE: Institut fur Pharmakologie, Universitatsklinikum Essen, Hufelandstrasse 55, D-45122 Essen, Germany.. meyer-heringdorf@uni-essen.de
CONTRACT NUMBER: 61469
SOURCE: FEBS letters, (2003 Nov 20) 554 (3) 443-9.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20031119
Last Updated on STN: 20031219
Entered Medline: 20031218

L13 ANSWER 28 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2003514059 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14592418
TITLE: **Sphingosine-1-phosphate** is a high-affinity ligand for the G protein-coupled receptor GPR6 from mouse and induces intracellular Ca2+ release by activating the **sphingosine-kinase** pathway.
AUTHOR: Ignatov Atanas; Lintzel Julia; Kreienkamp Hans-Jurgen; Schaller H Chica
CORPORATE SOURCE: Zentrum fur Molekulare Neurobiologie Hamburg, Universitat Hamburg, Martinistr. 52, D-22246 Hamburg, Germany.
SOURCE: Biochemical and biophysical research communications, (2003 Nov 14) 311 (2) 329-36.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20031101
Last Updated on STN: 20040211
Entered Medline: 20040210

L13 ANSWER 29 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2003432537 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12972327
TITLE: Agonist function of the neurokinin receptor antagonist, [D-Arg1,D-Phe5,D-Trp7,9,Leu11]substance P, in monocytes.
AUTHOR: Djanani Angela; Kaneider Nicole C; Sturn Daniel; Wiedermann Christian J
CORPORATE SOURCE: Department of Internal Medicine, Division of General Internal Medicine, University of Innsbruck, Anichstrasse 35, A-6020, Innsbruck, Austria.
SOURCE: Regulatory peptides, (2003 Sep 15) 115 (2) 123-9.
Journal code: 8100479. ISSN: 0167-0115.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20030916
Last Updated on STN: 20040529
Entered Medline: 20040528

L13 ANSWER 30 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2003426178 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12815058
TITLE: Role of **human sphingosine-1-phosphate** phosphatase 1 in the regulation of intra- and extracellular **sphingosine-1-phosphate** levels and cell viability.
AUTHOR: Johnson Korey R; Johnson Kristy Y; Becker Kevin P; Bielawski Jacek; Mao Cungui; Obeid Lina M
CORPORATE SOURCE: Department of Medicine, Medical University of South Carolina, Charleston, South Carolina 29425, USA.

CONTRACT NUMBER: 1P20RR17677 (NCRR)
GM62287 (NIGMS)
HL 07260 (NHLBI)
SOURCE: Journal of biological chemistry, (2003 Sep 5) 278 (36) 34541-7. Electronic Publication: 2003-06-18.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030912
Last Updated on STN: 20031008
Entered Medline: 20031007

L13 ANSWER 31 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2003364101 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12895655
TITLE: Leukocyte motility in response to neuropeptides is heparan sulfate proteoglycan dependent.
AUTHOR: Kaneider Nicole C; Egger Petra; Djanani Angela M; Wiedermann Christian J
CORPORATE SOURCE: Division of General Internal Medicine, Department of Internal Medicine, University of Innsbruck, Anichstrasse 35, A-6020 Innsbruck, Austria.
SOURCE: Peptides, (2003 May) 24 (5) 695-700.
Journal code: 8008690. ISSN: 0196-9781.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20030805
Last Updated on STN: 20040421
Entered Medline: 20040420

L13 ANSWER 32 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2003361849 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12890694
TITLE: The **sphingosine kinase** 1/ **sphingosine-1-phosphate** pathway mediates COX-2 induction and PGE2 production in response to TNF-alpha.
AUTHOR: Pettus Benjamin J; Bielawski Jacek; Porcelli Anna M; Reames Davis L; Johnson Korey R; Morrow Jason; Chalfant Charles E; Obeid Lina M; Hannun Yusuf A
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Medical University of South Carolina, Charleston, South Carolina 29425, USA.
CONTRACT NUMBER: CA77839 (NCI)
CA87584 (NCI)
DK48831 (NIDDK)
GM08716 (NIGMS)
GM15431 (NIGMS)
GM43825 (NIGMS)
GM62887 (NIGMS)
HL 07260 (NHLBI)
SOURCE: FASEB journal : official publication of the Federation of American Societies for Experimental Biology, (2003 Aug) 17 (11) 1411-21.
Journal code: 8804484. ISSN: 1530-6860.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20030805
Last Updated on STN: 20030812
Entered Medline:. 20030811

L13 ANSWER 33 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2003280908 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12682045
TITLE: Sphingosine phosphate lyase expression is essential for normal development in Caenorhabditis elegans.
AUTHOR: Mendel Jane; Heinecke Karie; Fyrst Henrik; Saba Julie D
CORPORATE SOURCE: Children's Hospital Oakland Research Institute, Oakland, California 94609-1673, USA.
CONTRACT NUMBER: 1R01CA77528 (NCI)
SOURCE: Journal of biological chemistry, (2003 Jun 20) 278 (25) 22341-9. Electronic Publication: 2003-04-07.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20030617
Last Updated on STN: 20030822
Entered Medline: 20030821

L13 ANSWER 34 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2003113624 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12626530
TITLE: Cutting edge: Mycobacterium tuberculosis blocks Ca2+ signaling and phagosome maturation in **human** macrophages via specific inhibition of **sphingosine kinase**.
AUTHOR: Malik Zulfiqar A; Thompson Christopher R; Hashimi Samad; Porter Brandon; Iyer Shankar S; Kusner David J
CORPORATE SOURCE: Inflammation Program, Graduate Program in Immunology, University of Iowa and Veterans Affairs Medical Center, Iowa City, IA 52242, USA.
CONTRACT NUMBER: R01 GM62302 (NIGMS)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2003 Mar 15) 170 (6) 2811-5.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20030311
Last Updated on STN: 20030626
Entered Medline: 20030625

L13 ANSWER 35 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2003036030 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12543093
TITLE: **Sphingosine 1-phosphate**: a Ca2+ release mediator in the balance.
AUTHOR: Young K W; Nahorski S R
CORPORATE SOURCE: Department of Cell Physiology and Pharmacology, Medical Sciences Building, University of Leicester, LE1 9HN, Leicester, UK.. kwyl@le.ac.uk
SOURCE: Cell calcium, (2002 Nov-Dec) 32 (5-6) 335-41. Ref: 36

Journal code: 8006226. ISSN: 0143-4160.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20030125
Last Updated on STN: 20030816
Entered Medline: 20030815

L13 ANSWER 36 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2003024553 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12531554
TITLE: **Sphingosine kinase, sphingosine -1-phosphate,** and apoptosis.
AUTHOR: Maceyka Michael; Payne Shawn G; Milstien Sheldon; Spiegel Sarah
CORPORATE SOURCE: Department of Biochemistry, Medical College of Virginia Campus, Virginia Commonwealth University, 1101 E. Marshall St., Richmond, VA 23298-0614, USA.
CONTRACT NUMBER: CA61774 (NCI)
GM43880 (NIGMS)
SOURCE: Biochimica et biophysica acta, (2002 Dec 30) 1585 (2-3) 193-201. Ref: 107
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030118
Last Updated on STN: 20030319
Entered Medline: 20030318

L13 ANSWER 37 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2003024548 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12531549
TITLE: Sphingosine in apoptosis signaling.
AUTHOR: Cuvillier Olivier
CORPORATE SOURCE: Inserm U466, Institut Louis Bugnard, CHU Rangueil, 1 avenue Jean Poulhes, 31403 Toulouse Cedex 4, France..
olivier.culliver@toulouse.inserm.fr
SOURCE: Biochimica et biophysica acta, (2002 Dec 30) 1585 (2-3) 153-62. Ref: 105
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030118
Last Updated on STN: 20030319
Entered Medline: 20030318

L13 ANSWER 38 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2003008597 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12485162

TITLE: Signalling mechanisms in **sphingosine 1-phosphate**-promoted mesangial cell proliferation.
AUTHOR: Katsuma Susumu; Hada Yuko; Ueda Toshihiro; Shiojima Satoshi; Hirasawa Akira; Tanoue Akito; Takagaki Kazuchika; Ohgi Tadaaki; Yano Junichi; Tsujimoto Gozoh
CORPORATE SOURCE: Department of Molecular, Cell Pharmacology, National Center for Child Health and Development Research Institute, 3-35-31, Taishido, Setagaya-Ku, Tokyo 154-8567, Japan.
SOURCE: Genes to cells : devoted to molecular & cellular mechanisms, (2002 Dec) 7 (12) 1217-30.
Journal code: 9607379. ISSN: 1356-9597.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20030108
Last Updated on STN: 20031218
Entered Medline: 20031217

L13 ANSWER 39 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2002731982 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12393916
TITLE: The nucleotide-binding site of **human sphingosine kinase** 1.
AUTHOR: Pitson Stuart M; Moretti Paul A B; Zebol Julia R; Zareie Reza; Derian Claudia K; Darrow Andrew L; Qi Jenson; D'Andrea Richard J; Bagley Christopher J; Vadas Mathew A; Wattenberg Binks W
CORPORATE SOURCE: Hanson Institute, Division of Human Immunology, Institute of Medical and Veterinary Science, Frome Road, Adelaide SA 5000, Australia.. stuart.pitson@imvs.sa.gov.asu
SOURCE: Journal of biological chemistry, (2002 Dec 20) 277 (51) 49545-53. Electronic Publication: 2002-10-18.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20021227
Last Updated on STN: 20030214
Entered Medline: 20030212

L13 ANSWER 40 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2002700454 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12444147
TITLE: **Sphingosine kinase**: a point of convergence in the action of diverse neutrophil priming agents.
AUTHOR: MacKinnon Alison C; Buckley Avril; Chilvers Edwin R; Rossi Adriano G; Haslett Christopher; Sethi Tariq
CORPORATE SOURCE: Lung Inflammatory Group, Center for Inflammation Research, University of Edinburgh, United Kingdom.. a.mackinnon@ed.ac.uk
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2002 Dec 1) 169 (11) 6394-400.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200212

ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20021227
Entered Medline: 20021224

L13 ANSWER 41 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2002680929. MEDLINE
DOCUMENT NUMBER: PubMed ID: 12441135
TITLE: **Sphingosine kinase** type 1 promotes estrogen-dependent tumorigenesis of breast cancer MCF-7 cells.
AUTHOR: Nava Victor E; Hobson John Peyton; Murthy Shvetha; Milstien Sheldon; Spiegel Sarah
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC 20007, USA.
CONTRACT NUMBER: CA61774 (NCI)
SOURCE: Experimental cell research, (2002 Nov 15) 281 (1) 115-27. Journal code: 0373226. ISSN: 0014-4827.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021121
Last Updated on STN: 20021217
Entered Medline: 20021212

L13 ANSWER 42 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2002485445 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12124383
TITLE: PKC-dependent activation of **sphingosine kinase** 1 and translocation to the plasma membrane. Extracellular release of **sphingosine-1-phosphate** induced by phorbol 12-myristate 13-acetate (PMA).
AUTHOR: Johnson Korey R; Becker Kevin P; Facchinetti Maria Marta; Hannun Yusuf A; Obeid Lina M
CORPORATE SOURCE: Department of Medicine, Medical University of South Carolina, Charleston, South Carolina 29425, USA.
CONTRACT NUMBER: GM62887 (NIGMS)
HL07260 (NHLBI)
HL43707 (NHLBI)
SOURCE: Journal of biological chemistry, (2002 Sep 20) 277 (38) 35257-62. Electronic Publication: 2002-07-17. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020926
Last Updated on STN: 20030105
Entered Medline: 20021024

L13 ANSWER 43 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2002447609 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12204793
TITLE: D-erythro-N,N-dimethylsphingosine inhibits bFGF-induced proliferation of cerebral, aortic and coronary smooth muscle cells.
AUTHOR: Xu Cang-Bao; Zhang Yaping; Stenman Emelie; Edvinsson Lars
CORPORATE SOURCE: Department of Medicine, Lund University, Division of Experimental Vascular Research, S-22185, Lund, Sweden.

SOURCE: Atherosclerosis, (2002 Oct) 164 (2) 237-43.
Journal code: 0242543. ISSN: 0021-9150.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20020904
Last Updated on STN: 20030207
Entered Medline: 20030206

L13 ANSWER 44 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2002442792 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12200669
TITLE: **Sphingosine 1-phosphate** as a therapeutic agent.
AUTHOR: Spiegel S; Kolesnick R
CORPORATE SOURCE: Department of Biochemistry, Medical College of Virginia Campus, Virginia Commonwealth University, Richmond, VA 23298-0614, USA.
CONTRACT NUMBER: CA42385 (NCI)
CA85704 (NCI)
GM43880 (NIGMS)
SOURCE: Leukemia : official journal of the Leukemia Society of America, Leukemia Research Fund, U.K, (2002 Sep) 16 (9) 1596-602. Ref: 79
Journal code: 8704895. ISSN: 0887-6924.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020830
Last Updated on STN: 20020927
Entered Medline: 20020926

L13 ANSWER 45 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2002372411 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12011102
TITLE: **Sphingosine 1-phosphate**, a key cell signaling molecule.
AUTHOR: Spiegel Sarah; Milstien Sheldon
CORPORATE SOURCE: Department of Biochemistry, Medical College of Virginia Campus, Virginia Commonwealth University, Richmond, Virginia 23298-0614, USA.. sspiegel@mail1.vcu.edu
CONTRACT NUMBER: CA61774 (NCI)
GM43880 (NIGMS)
SOURCE: Journal of biological chemistry, (2002 Jul 19) 277 (29) 25851-4. Electronic Publication: 2002-05-13. Ref: 73
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020716
Last Updated on STN: 20030105
Entered Medline: 20020906

L13 ANSWER 46 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2002359120 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12102559
TITLE: **Sphingosine kinases**: a novel family of lipid **kinases**.
AUTHOR: Liu Hong; Chakravarty Debyani; Maceyka Michael; Milstien Sheldon; Spiegel Sarah
CORPORATE SOURCE: Department of Biochemistry, Virginia Commonwealth University, Richmond 23298, USA.
CONTRACT NUMBER: CA61774 (NCI)
GM43880 (NIGMS)
SOURCE: Progress in nucleic acid research and molecular biology, (2002) 71 493-511. Ref: 85
Journal code: 0102753. ISSN: 0079-6603.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20020710
Last Updated on STN: 20030130
Entered Medline: 20030129

L13 ANSWER 47 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2002327040 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12069819
TITLE: **Sphingosine 1-phosphate** signalling and termination at lipid phosphate receptors.
AUTHOR: Pyne Susan; Pyne Nigel J
CORPORATE SOURCE: Department of Physiology and Pharmacology, Strathclyde Institute for Biomedical Sciences, University of Strathclyde, 27 Taylor Street, Scotland, Glasgow, UK.. susan.pyne@strath.ac.uk
SOURCE: Biochimica et biophysica acta, (2002 May 23) 1582 (1-3) 121-31. Ref: 85
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020619
Last Updated on STN: 20020823
Entered Medline: 20020822

L13 ANSWER 48 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2002214119 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11950216
TITLE: Simultaneous quantitative analysis of sphingoid base 1-phosphates in biological samples by o-phthalaldehyde precolumn derivatization after dephosphorylation with alkaline phosphatase.
AUTHOR: Min Jung-Kee; Yoo Hwan-Soo; Lee Eun-Young; Lee Woo-Jin; Lee Yong-Moon
CORPORATE SOURCE: College of Pharmacy, Chungbuk National University, Chongju 361-763, South Korea.
SOURCE: Analytical biochemistry, (2002 Apr 15) 303 (2) 167-75.
Journal code: 0370535. ISSN: 0003-2697.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020413
Last Updated on STN: 20020605
Entered Medline: 20020604

L13 ANSWER 49 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2002203890 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11936187
TITLE: Fibronectin promotes calcium signaling by interferon-gamma in **human** neutrophils via G-protein and **sphingosine kinase**-dependent mechanisms.
AUTHOR: Aas V; Algeroy S; Sand K L; Iversen J G
CORPORATE SOURCE: Department of Pharmacology, School of Pharmacy, University of Oslo, Norway.. vigdisaa@farmasi.uio.no
SOURCE: Cell communication & adhesion, (2001) 8 (3) 125-38.
Journal code: 101096596. ISSN: 1541-9061.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20020409
Last Updated on STN: 20021211
Entered Medline: 20040416

L13 ANSWER 50 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2002183955 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11915350
TITLE: Molecular diversity of **sphingosine kinase**
AUTHOR: Tsukahara Tamotsu; Mizuno Hirotaka; Igarashi Yasuyukitsuka@kinou02.pharm.hokudai.ac.jp
SOURCE: Tanpakushitsu kakusan koso. Protein, nucleic acid, enzyme, (2002 Mar) 47 (4 Suppl) 509-13. Ref: 13
Journal code: 0413762. ISSN: 0039-9450.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020403
Last Updated on STN: 20020417
Entered Medline: 20020416

L13 ANSWER 51 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2002130081 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11741921
TITLE: Extracellular export of **sphingosine kinase**-1 enzyme. **Sphingosine 1-phosphate** generation and the induction of angiogenic vascular maturation.
AUTHOR: Ancellin Nicolas; Colmont Chantal; Su Joseph; Li Qin; Mittereder Nanette; Chae Sung-Suk; Stefansson Steingrimur; Liau Gene; Hla Timothy
CORPORATE SOURCE: Center for Vascular Biology, Department of Physiology, University of Connecticut Health Center, Farmington, Connecticut 06030-3501, USA.
CONTRACT NUMBER: DK45659 (NIDDK)
HL67330 (NHLBI)

SOURCE: Journal of biological chemistry, (2002 Feb 22) 277 (8) 6667-75. Electronic Publication: 2001-12-10.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020228
Last Updated on STN: 20030105
Entered Medline: 20020424

L13 ANSWER 52 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001665927 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11710939
TITLE: 1Alpha,25-dihydroxyvitamin D3 protects **human** keratinocytes from apoptosis by the formation of **sphingosine-1-phosphate**.
AUTHOR: Manggau M; Kim D S; Ruwisch L; Vogler R; Korting H C; Schafer-Korting M; Kleuser B
CORPORATE SOURCE: Institut fur Pharmazie, Abteilung fur Pharmakologie, Freie Universitat Berlin, Berlin, Germany.
SOURCE: Journal of investigative dermatology, (2001 Nov) 117 (5) 1241-9.
Journal code: 0426720. ISSN: 0022-202X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011119
Last Updated on STN: 20020123
Entered Medline: 20011220

L13 ANSWER 53 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001663606 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11709084
TITLE: The **sphingosine-1-phosphate** receptor EDG-1 is essential for platelet-derived growth factor-induced cell motility.
AUTHOR: Rosenfeldt H M; Hobson J P; Milstien S; Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC 20007, USA.
SOURCE: Biochemical Society transactions, (2001 Nov) 29 (Pt 6) 836-9.
Journal code: 7506897. ISSN: 0300-5127.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20011119
Last Updated on STN: 20020313
Entered Medline: 20020312

L13 ANSWER 54 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001568136 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11675357
TITLE: **Sphingosine 1-phosphate** antagonizes apoptosis of **human** leukemia cells by inhibiting release of cytochrome c and Smac/DIABLO from mitochondria.

AUTHOR: Cuvillier O; Levade T
CORPORATE SOURCE: Inserm U466, Toulouse, France..
olivier.cuvillier@rangueil.inserm.fr
SOURCE: Blood, (2001 Nov 1) 98 (9) 2828-36.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011025
Last Updated on STN: 20020122
Entered Medline: 20011207

L13 ANSWER 55 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001504463 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11258664
TITLE: Activation of **sphingosine kinase** by the bradykinin B2 receptor and its implication in regulation of the ERK/MAP **kinase** pathway.
AUTHOR: Blaukat A; Dikic I
CORPORATE SOURCE: Pharmakologisches Institut, Ruprecht-Karls-Universitat Heidelberg, Germany.
SOURCE: Biological chemistry, (2001 Jan) 382 (1) 135-9.
Journal code: 9700112. ISSN: 1431-6730.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010917
Last Updated on STN: 20010917
Entered Medline: 20010913

L13 ANSWER 56 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001476974 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11520048
TITLE: **Sphingosine kinase** regulates hepatoma cell differentiation: roles of hepatocyte nuclear factor and retinoid receptor.
AUTHOR: Osawa Y; Nagaki M; Banno Y; Nozawa Y; Moriwaki H; Nakashima S
CORPORATE SOURCE: First Department of Internal Medicine, Gifu University School of Medicine, Tsukasamachi-40, Gifu 500-8705, Japan.
SOURCE: Biochemical and biophysical research communications, (2001 Aug 31) 286 (4) 673-7.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010827
Last Updated on STN: 20030204
Entered Medline: 20010927

L13 ANSWER 57 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001381154 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10880336
TITLE: **Sphingosine 1-phosphate** signalling in mammalian cells.
AUTHOR: Pyne S; Pyne N J
CORPORATE SOURCE: Department of Physiology and Pharmacology, Strathclyde

Institute for Biomedical Sciences, University of Strathclyde, 27 Taylor Street, Glasgow G4 ONR, Scotland, UK.. susan.pyne@strath.ac.uk
SOURCE: Biochemical journal, (2000 Jul 15) 349 (Pt 2) 385-402. Ref: 174
Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20010709
Entered Medline: 20010705

L13 ANSWER 58 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001364644 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11418646
TITLE: TNF-alpha-induced **sphingosine 1-phosphate** inhibits apoptosis through a phosphatidylinositol 3-**kinase**/Akt pathway in **human** hepatocytes.
AUTHOR: Osawa Y; Banno Y; Nagaki M; Brenner D A; Naiki T; Nozawa Y; Nakashima S; Moriwaki H
CORPORATE SOURCE: First Department of Internal Medicine and Department of Biochemistry, Gifu University School of Medicine, Gifu, Japan.
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2001 Jul 1) 167 (1) 173-80.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010924
Last Updated on STN: 20010924
Entered Medline: 20010920

L13 ANSWER 59 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001354177 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11239914
TITLE: Stimulation of intracellular **sphingosine-1-phosphate** production by G-protein-coupled **sphingosine-1-phosphate** receptors.
AUTHOR: Meyer zu Heringdorf D; Lass H; Kuchar I; Lipinski M; Alemany R; Rumenapp U; Jakobs K H
CORPORATE SOURCE: Institut fur Pharmakologie, Universitatsklinikum Essen, Hufelandstrasse 55, D-45122 Essen, Germany.. meyer-heringdorf@uni-essen.de
SOURCE: European journal of pharmacology, (2001 Mar 2) 414 (2-3) 145-54.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010625
Last Updated on STN: 20020919
Entered Medline: 20010621

L13 ANSWER 60 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001319046 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11392623
TITLE: **Sphingosine kinase**-mediated calcium signaling by muscarinic acetylcholine receptors.
AUTHOR: van Koppen C J; Meyer zu Heringdorf D; Alemany R; Jakobs K H
CORPORATE SOURCE: Institut fur Pharmakologie, Universitatsklinikum Essen, Germany.. van_koppen@uni-essen.de
SOURCE: Life sciences, (2001 Apr 27) 68 (22-23) 2535-40. Journal code: 0375521. ISSN: 0024-3205.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010625
Last Updated on STN: 20010625
Entered Medline: 20010621

L13 ANSWER 61 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001286242 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11284453
TITLE: An improved high-performance liquid chromatographic method for the determination of **sphingosine-1-phosphate** in complex biological materials.
AUTHOR: Ruwisch L; Schafer-Korting M; Kleuser B
CORPORATE SOURCE: Institut fur Pharmazie, Pharmakologie und Toxikologie, Freie Universitat Berlin, Germany.
SOURCE: Naunyn-Schmiedeberg's archives of pharmacology, (2001 Mar) 363 (3) 358-63. Journal code: 0326264. ISSN: 0028-1298.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20010529
Entered Medline: 20010524

L13 ANSWER 62 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001198695 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11230698
TITLE: Role of the **sphingosine-1-phosphate** receptor EDG-1 in PDGF-induced cell motility.
AUTHOR: Hobson J P; Rosenfeldt H M; Barak L S; Olivera A; Poulton S; Caron M G; Milstien S; Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC 20007, USA.
CONTRACT NUMBER: CA61774 (NCI)
GM43880 (NIGMS)
HL-61365 (NHLBI)
NS19576 (NINDS)
SOURCE: Science, (2001 Mar 2) 291 (5509) 1800-3. Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010410
Last Updated on STN: 20010410
Entered Medline: 20010405

L13 ANSWER 63 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001182497 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11166272
TITLE: Platelet-released phospholipids link haemostasis and angiogenesis.
AUTHOR: English D; Garcia J G; Brindley D N
CORPORATE SOURCE: Experimental Cell Research Program, Methodist Research Institute, 1701 N. Senate, Rm. 1417 MPC, Indianapolis, IN 46202, USA.. dkenglish@msn.com
CONTRACT NUMBER: PO1 HL 58064 (NHLBI)
RO1 HL 61751 (NHLBI)
SOURCE: Cardiovascular research, (2001 Feb 16) 49 (3) 588-99. Ref: 54
Journal code: 0077427. ISSN: 0008-6363.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010329

L13 ANSWER 64 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001115700 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11114522
TITLE: An oncogenic role of **sphingosine kinase**
AUTHOR: Xia P; Gamble J R; Wang L; Pitson S M; Moretti P A; Wattenberg B W; D'Andrea R J; Vadas M A
CORPORATE SOURCE: Division of Human Immunology, Hanson Centre for Cancer Research, Institute of Medical and Veterinary Science and University of Adelaide, Frome Road, SA 5000,., Adelaide, Australia.. pu.xia@imvs.sa.gov.au
SOURCE: Current biology : CB, (2000 Nov 30) 10 (23) 1527-30.
Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010215

L13 ANSWER 65 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001108699 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11115407
TITLE: Extracellular mechanism through the Edg family of receptors might be responsible for **sphingosine-1-phosphate**-induced regulation of DNA synthesis and migration of rat aortic smooth-muscle cells.
AUTHOR: Tamama K; Kon J; Sato K; Tomura H; Kuwabara A; Kimura T; Kanda T; Ohta H; Ui M; Kobayashi I; Okajima F
CORPORATE SOURCE: Laboratory of Signal Transduction, Institute for Molecular and Cellular Regulation, Gunma University, 3-39-15 Showa-machi, Maebashi 371-8512, Japan.

SOURCE: Biochemical journal, (2001 Jan 1) 353 (Pt 1) 139-146.
Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010208

L13 ANSWER 66 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001107842 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11150592
TITLE: **Sphingosine 1-phosphate** signalling via the endothelial differentiation gene family of G-protein-coupled receptors.
AUTHOR: Pyne S; Pyne N
CORPORATE SOURCE: Department of Physiology and Pharmacology, Strathclyde Institute for Biomedical Sciences, University of Strathclyde, 27 Taylor Street, G4 ONR Scotland, Glasgow, UK.. susan.pyne@strath.ac.uk
SOURCE: Pharmacology & therapeutics, (2000 Nov) 88 (2) 115-31.
Ref: 123
Journal code: 7905840. ISSN: 0163-7258.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010208

L13 ANSWER 67 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001088872 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10954727
TITLE: Lysophosphatidic acid-induced Ca2+ mobilization requires intracellular **sphingosine 1-phosphate** production. Potential involvement of endogenous EDG-4 receptors.
AUTHOR: Young K W; Bootman M D; Channing D R; Lipp P; Maycox P R; Meakin J; Challiss R A; Nahorski S R
CORPORATE SOURCE: Department of Cell Physiology and Pharmacology, Medical Sciences Building, University of Leicester, University Road, Leicester, LE1 9HN United Kingdom.
SOURCE: Journal of biological chemistry, (2000 Dec 8) 275 (49) 38532-9.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010118

L13 ANSWER 68 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001056248 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11079797

TITLE: Characterization of B-5354c, a new **sphingosine kinase** inhibitor, produced by a marine bacterium.
AUTHOR: Kono K; Tanaka M; Ogita T; Kohama T
CORPORATE SOURCE: Pharmacology and Molecular Biology Research Laboratories, Research Institute, Sankyo Co., Ltd., Shinagawa, Tokyo, Japan.
SOURCE: Journal of antibiotics, (2000 Aug) 53 (8) 759-64.
Journal code: 0151115. ISSN: 0021-8820.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001215

L13 ANSWER 69 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2001038285 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10944534
TITLE: Expression of a catalytically inactive **sphingosine kinase** mutant blocks agonist-induced **sphingosine kinase** activation. A dominant-negative **sphingosine kinase**.
AUTHOR: Pitson S M; Moretti P A; Zebol J R; Xia P; Gamble J R; Vadas M A; D'Andrea R J; Wattenberg B W
CORPORATE SOURCE: Hanson Centre for Cancer Research, Division of Human Immunology, Institute of Medical and Veterinary Science and the Department of Medicine, University of Adelaide, Frome Road, Adelaide, SA 5000, Australia.
SOURCE: Journal of biological chemistry, (2000 Oct 27) 275 (43) 33945-50.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001124

L13 ANSWER 70 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000513637 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11070858
TITLE: Enzymatic method for measurement of **sphingosine 1-phosphate**.
AUTHOR: Edsall L; Vann L; Milstien S; Spiegel S
CORPORATE SOURCE: Laboratory of Molecular and Cellular Regulation, National Institute of Mental Health, Bethesda, Maryland 20892, USA.
CONTRACT NUMBER: CA61774 (NCI)
GM43880 (NIGMS)
SOURCE: Methods in enzymology, (2000) 312 9-16.
Journal code: 0212271. ISSN: 0076-6879.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010301

L13 ANSWER 71 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000482537 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10940357
TITLE: Effect of dimethylsphingosine on muscarinic M(3) receptor signalling in SH-SY5Y cells.
AUTHOR: Young K W; Channing D R; Nahorski S R
CORPORATE SOURCE: Department of Cell Physiology and Pharmacology, Medical Sciences Building, University of Leicester, University Road, Leicester LE1 9HN, UK.. kwy1@le.ac.uk
SOURCE: European journal of pharmacology, (2000 Aug 18) 402 (1-2) 55-9.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001019
Last Updated on STN: 20001019
Entered Medline: 20001011

L13 ANSWER 72 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000470689 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10859593
TITLE: Diverse effects of sphingosine on calcium mobilization and influx in differentiated HL-60 cells.
AUTHOR: Shin Y; Daly J W; Choi O H
CORPORATE SOURCE: Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive Disorder of Kidney, National Institutes of Health, Bethesda, Maryland, USA.
CONTRACT NUMBER: RR03032 (NCRR)
SOURCE: Cell calcium, (2000 May) 27 (5) 269-80.
Journal code: 8006226. ISSN: 0143-4160.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001012
Last Updated on STN: 20001012
Entered Medline: 20001002

L13 ANSWER 73 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000459903 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10953041
TITLE: Stimulation of **sphingosine-1-phosphate** formation by the P2Y(2) receptor in HL-60 cells: Ca(2+) requirement and implication in receptor-mediated Ca(2+) mobilization, but not MAP **kinase** activation.
AUTHOR: Alemany R; Sichelschmidt B; zu Heringdorf D M; Lass H; van Koppen C J; Jakobs K H
CORPORATE SOURCE: Institut fur Pharmakologie, Universitatsklinikum Essen, Essen, Germany.
SOURCE: Molecular pharmacology, (2000 Sep) 58 (3) 491-7.
Journal code: 0035623. ISSN: 0026-895X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20001005
Last Updated on STN: 20001005

Entered Medline: 20000925

L13 ANSWER 74 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000426007 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10969794
TITLE: Sphingosine enhances apoptosis of radiation-resistant prostate cancer cells.
AUTHOR: Nava V E; Cuvillier O; Edsall L C; Kimura K; Milstien S; Gelmann E P; Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC 20007, USA.
CONTRACT NUMBER: CA/AG79912 (NCI)
CA61774 (NCI)
SOURCE: Cancer research, (2000 Aug 15) 60 (16) 4468-74.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000914

L13 ANSWER 75 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000399757 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10847608
TITLE: A high-performance liquid chromatographic method to measure **sphingosine 1-phosphate** and related compounds from **sphingosine kinase** assays and other biological samples.
AUTHOR: Caligan T B; Peters K; Ou J; Wang E; Saba J; Merrill A H Jr
CORPORATE SOURCE: Department of Biochemistry, Emory University School of Medicine, Atlanta, Georgia 30322, USA.
CONTRACT NUMBER: CA77528-01 (NCI)
GM46368 (NIGMS)
SOURCE: Analytical biochemistry, (2000 May 15) 281 (1) 36-44.
Journal code: 0370535. ISSN: 0003-2697.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000816

L13 ANSWER 76 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000387082 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10751414
TITLE: Molecular cloning and functional characterization of a novel mammalian **sphingosine kinase** type 2 isoform.
AUTHOR: Liu H; Sugiura M; Nava V E; Edsall L C; Kono K; Poulton S; Milstien S; Kohama T; Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, D. C. 20007, USA.
CONTRACT NUMBER: GM43880 (NIGMS)
SOURCE: Journal of biological chemistry, (2000 Jun 30) 275 (26) 19513-20.
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF245447; GENBANK-AF245448
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000818
Last Updated on STN: 20000818
Entered Medline: 20000810

L13 ANSWER 77 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000278413 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10818472
TITLE: Endothelin-1 stimulates **sphingosine kinase** in **human** hepatic stellate cells. A novel role for sphingosine-1-P as a mediator of growth inhibition.
AUTHOR: Gallois C; Davaille J; Habib A; Mallat A; Tao J; Levade T; Lotersztajn S
CORPORATE SOURCE: INSERM U99, Hopital Henri Mondor, Creteil, France.
SOURCE: Annals of the New York Academy of Sciences, (2000 Apr) 905 311-4.
Journal code: 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000616
Last Updated on STN: 20000616
Entered Medline: 20000605

L13 ANSWER 78 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000267921 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10806317
TITLE: Sphingomyelinase metabolites control survival and apoptotic death in SH-SY5Y neuroblastoma cells.
AUTHOR: Tavarini S; Colombaioni L; Garcia-Gil M
CORPORATE SOURCE: Departments of Physiology and Biochemistry, University of Pisa, via S. Zeno 31, 56127, Pisa, Italy.
SOURCE: Neuroscience letters, (2000 May 19) 285 (3) 185-8.
Journal code: 7600130. ISSN: 0304-3940.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000811
Last Updated on STN: 20000811
Entered Medline: 20000801

L13 ANSWER 79 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000263733 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10802064
TITLE: Functional characterization of **human sphingosine kinase**-1.
AUTHOR: Nava V E; Lacana E; Poulton S; Liu H; Sugiura M; Kono K; Milstien S; Kohama T; Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, 353 Basic Science Building, 3900 Reservoir Road NW, Washington, DC 20007, USA.
CONTRACT NUMBER: GM43880 (NIGMS).

SOURCE: FEBS letters, (2000 May 4) 473 (1) 81-4.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF238083
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000616
Last Updated on STN: 20000616
Entered Medline: 20000605

L13 ANSWER 80 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000225422 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10760461
TITLE: Functions of a new family of **sphingosine-1-phosphate** receptors.
AUTHOR: Spiegel S; Milstien S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC 20007, USA.. spiegel@bc.georgetown.edu
CONTRACT NUMBER: CA61774 (NCI)
GM43880 (NIGMS)
SOURCE: Biochimica et biophysica acta, (2000 Apr 12) 1484 (2-3) 107-16. Ref: 93
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000706
Last Updated on STN: 20020919
Entered Medline: 20000623

L13 ANSWER 81 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000127766 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10666000
TITLE: Tumor necrosis factor-alpha-mediated signal transduction in **human** neutrophils: involvement of sphingomyelin metabolites in the priming effect of TNF-alpha on the fMLP-stimulated superoxide production.
AUTHOR: Niwa M; Kozawa O; Matsuno H; Kanamori Y; Hara A; Uematsu T
CORPORATE SOURCE: Department of Pharmacology, Gifu University School of Medicine, Japan.. mniwa@cc.gifu-u.ac.jp
SOURCE: Life sciences, (2000) 66 (3) 245-56.
Journal code: 0375521. ISSN: 0024-3205.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000229
Last Updated on STN: 20000229
Entered Medline: 20000217

L13 ANSWER 82 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000090237 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10626811
TITLE: **Sphingosine-1-phosphate** inhibits motility of **human** breast cancer cells

independently of cell surface receptors.
AUTHOR: Wang F; Van Brocklyn J R; Edsall L; Nava V E; Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC 20007, USA.
CONTRACT NUMBER: CA61774 (NCI)
F32 GM19209 (NIGMS)
GM 39718 (NIGMS)
SOURCE: Cancer research, (1999 Dec 15) 59 (24) 6185-91.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000204
Last Updated on STN: 20000204
Entered Medline: 20000124

L13 ANSWER 83 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000036602 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10567432
TITLE: Activation of **sphingosine kinase** by tumor necrosis factor-alpha inhibits apoptosis in **human** endothelial cells.
AUTHOR: Xia P; Wang L; Gamble J R; Vadas M A
CORPORATE SOURCE: Division of Human Immunology, The Hanson Centre for Cancer Research, Adelaide, South Australia 5000, Australia.
SOURCE: Journal of biological chemistry, (1999 Nov 26) 274 (48) 34499-505.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991229

L13 ANSWER 84 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000036448 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10567700
TITLE: Role of **sphingosine kinase** in Ca(2+) signalling by epidermal growth factor receptor.
AUTHOR: Meyer zu Heringdorf D; Lass H; Kuchar I; Alemany R; Guo Y; Schmidt M; Jakobs K H
CORPORATE SOURCE: Institut fur Pharmakologie, Universitatsklinikum Essen, Hufelandstrasse 55, D-45122, Essen, Germany.. meyer-heringdorf@uni-essen.de
SOURCE: FEBS letters, (1999 Nov 19) 461 (3) 217-22.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991228

L13 ANSWER 85 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000023403 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10560747
TITLE: Structure-activity relationship of short-chain sphingoid bases as inhibitors of **sphingosine kinase**

AUTHOR: De Jonghe S; Van Overmeire I; Poulton S; Hendrix C; Busson R; Van Calenbergh S; De Keukeleire D; Spiegel S; Herdewijn P
CORPORATE SOURCE: University of Gent, Faculty of Pharmaceutical Sciences, Laboratory for Medicinal Chemistry, Belgium.
CONTRACT NUMBER: CA61774 (NCI)
GM43880 (NIGMS)
SOURCE: Bioorganic & medicinal chemistry letters, (1999 Nov 1) 9 (21) 3175-80.
Journal code: 9107377. ISSN: 0960-894X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991209

L13 ANSWER 86 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000020293 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10551885
TITLE: High density lipoproteins (HDL) interrupt the **sphingosine kinase** signaling pathway. A possible mechanism for protection against atherosclerosis by HDL.
AUTHOR: Xia P; Vadas M A; Rye K A; Barter P J; Gamble J R
CORPORATE SOURCE: Division of Human Immunology, Hanson Centre for Cancer Research, Institute of Medical Science, University of Adelaide, Adelaide, South Australia 5000, Australia.
SOURCE: Journal of biological chemistry, (1999 Nov 12) 274 (46) 33143-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000103

L13 ANSWER 87 OF 126 MEDLINE on STN
ACCESSION NUMBER: 2000014994 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10545499
TITLE: **Sphingosine kinase** expression increases intracellular **sphingosine-1-phosphate** and promotes cell growth and survival.
AUTHOR: Olivera A; Kohama T; Edsall L; Nava V; Cuvillier O; Poulton S; Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, District of Columbia 20007, USA.
CONTRACT NUMBER: RO1 GM43880 (NIGMS)
SOURCE: Journal of cell biology, (1999 Nov 1) 147 (3) 545-58.
Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20021218
Entered Medline: 19991124

L13 ANSWER 88 OF 126 MEDLINE on STN
ACCESSION NUMBER: 1999425067 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10493910
TITLE: Lysophosphatidic acid-mediated Ca2+ mobilization in **human** SH-SY5Y neuroblastoma cells is independent of phosphoinositide signalling, but dependent on **sphingosine kinase** activation.
AUTHOR: Young K W; Challiss R A; Nahorski S R; MacKrill J J
CORPORATE SOURCE: Department of Cell Physiology and Pharmacology, Medical Sciences Building, University of Leicester, P.O. Box 138, University Road, Leicester LE1 9HN, U.K.. kwy1@le.ac.uk
SOURCE: Biochemical journal, (1999 Oct 1) 343 Pt 1 45-52.
Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991207

L13 ANSWER 89 OF 126 MEDLINE on STN
ACCESSION NUMBER: 1999348274 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10419457
TITLE: Role of **sphingosine 1-phosphate** in the mitogenesis induced by oxidized low density lipoprotein in smooth muscle cells via activation of sphingomyelinase, ceramidase, and **sphingosine kinase**.
AUTHOR: Auge N; Nikolova-Karakashian M; Carpentier S; Parthasarathy S; Negre-Salvayre A; Salvayre R; Merrill A H Jr; Levade T
CORPORATE SOURCE: Laboratoire de Biochimie, INSERM U. 466, Universite Paul Sabatier, CHU Rangueil, 31403 Toulouse, France.. levade@rangueil.inserm.fr
CONTRACT NUMBER: GM 46368 (NIGMS)
SOURCE: Journal of biological chemistry, (1999 Jul 30) 274 (31) 21533-8.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990819

L13 ANSWER 90 OF 126 MEDLINE on STN
ACCESSION NUMBER: 1999335342 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10405296
TITLE: Enzymatic measurement of **sphingosine 1-phosphate**.
AUTHOR: Edsall L C; Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University, Medical Center, Washington, DC 20007, USA.

CONTRACT NUMBER: 1RO1 GM43880 (NIGMS)
SOURCE: Analytical biochemistry, (1999 Jul 15) 272 (1) 80-6.
Journal code: 0370535. ISSN: 0003-2697.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990925
Last Updated on STN: 19990925
Entered Medline: 19990910

L13 ANSWER 91 OF 126 MEDLINE on STN
ACCESSION NUMBER: 1999321844 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10393324
TITLE: **Sphingosine 1-phosphate** formation and intracellular Ca2+ mobilization in **human** platelets: evaluation with **sphingosine kinase** inhibitors.
AUTHOR: Yang L; Yatomi Y; Satoh K; Igarashi Y; Ozaki Y
CORPORATE SOURCE: Department of Laboratory Medicine, Yamanashi Medical University, Nakakoma, Yamanashi, 409-3898, Japan.
SOURCE: Journal of biochemistry, (1999 Jul) 126 (1) 84-9.
Journal code: 0376600. ISSN: 0021-924X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991028

L13 ANSWER 92 OF 126 MEDLINE on STN
ACCESSION NUMBER: 1999178622 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10080537
TITLE: **Sphingosine 1-phosphate**: a prototype of a new class of second messengers.
AUTHOR: Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC 20007, USA.. spiegel@bc.georgetown.edu
CONTRACT NUMBER: CA61774 (NCI)
GM43880 (NIGMS)
SOURCE: Journal of leukocyte biology, (1999 Mar) 65 (3) 341-4.
Ref: 41
Journal code: 8405628. ISSN: 0741-5400.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990413
Last Updated on STN: 19990413
Entered Medline: 19990401

L13 ANSWER 93 OF 126 MEDLINE on STN
ACCESSION NUMBER: 1999134321 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9933590
TITLE: Formyl peptide receptor signaling in HL-60 cells through **sphingosine kinase**.

AUTHOR: Alemany R; Meyer zu Heringdorf D; van Koppen C J; Jakobs K H
CORPORATE SOURCE: Institut fur Pharmakologie, Universitatsklinikum Essen, D-45122 Essen, Germany.
SOURCE: Journal of biological chemistry, (1999 Feb 12) 274 (7) 3994-9.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990324
Last Updated on STN: 20000303
Entered Medline: 19990311

L13 ANSWER 94 OF 126 MEDLINE on STN
ACCESSION NUMBER: 1999045661 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9826677
TITLE: Tumor necrosis factor-alpha induces adhesion molecule expression through the **sphingosine kinase** pathway.
AUTHOR: Xia P; Gamble J R; Rye K A; Wang L; Hii C S; Cockerill P; Khew-Goodall Y; Bert A G; Barter P J; Vadas M A
CORPORATE SOURCE: Division of Human Immunology, The Hanson Centre for Cancer Research, Institute of Medical and Veterinary Science and University of Adelaide, Adelaide, SA 5000, Australia.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1998 Nov 24) 95 (24) 14196-201.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981228

L13 ANSWER 95 OF 126 MEDLINE on STN
ACCESSION NUMBER: 1998409444 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9737868
TITLE: N,N-Dimethylsphingosine is a potent competitive inhibitor of **sphingosine kinase** but not of protein **kinase** C: modulation of cellular levels of **sphingosine 1-phosphate** and ceramide.
AUTHOR: Edsall L C; Van Brocklyn J R; Cuvillier O; Kleuser B; Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, D.C. 20007, USA.
CONTRACT NUMBER: CA61774 (NCI)
GM43880 (NIGMS)
SOURCE: Biochemistry, (1998 Sep 15) 37 (37) 12892-8.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981029
Last Updated on STN: 19981029

Entered Medline: 19981020

L13 ANSWER 96 OF 126 MEDLINE on STN
ACCESSION NUMBER: 1998332936 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9668339
TITLE: **Sphingosine-1-phosphate** in cell growth and cell death.
AUTHOR: Spiegel S; Cuvillier O; Edsall L C; Kohama T; Menzeleev R; Olah Z; Olivera A; Pirianov G; Thomas D M; Tu Z; Van Brocklyn J R; Wang F
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC 20007, USA.. spiegel@biochem1.basic-sci.georgetown.edu
CONTRACT NUMBER: RO1CA61774 (NCI)
RO1GM43880 (NIGMS)
SOURCE: Annals of the New York Academy of Sciences, (1998 Jun 19) 845 11-8. Ref: 52
Journal code: 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980817
Last Updated on STN: 19980817
Entered Medline: 19980804

L13 ANSWER 97 OF 126 MEDLINE on STN
ACCESSION NUMBER: 1998288261 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9624115
TITLE: Survival by Mac-1-mediated adherence and anoikis in phorbol ester-treated HL-60 cells.
AUTHOR: Nakamura H; Oda T; Hamada K; Hirano T; Shimizu N; Utiyama H
CORPORATE SOURCE: Life Science Group, Faculty of Integrated Arts and Sciences, Hiroshima University, Kagamiyama 1-7-1, Higashi-Hiroshima 739-8521, Japan.
SOURCE: Journal of biological chemistry, (1998 Jun 19) 273 (25) 15345-51.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980716
Last Updated on STN: 19980716
Entered Medline: 19980709

L13 ANSWER 98 OF 126 MEDLINE on STN
ACCESSION NUMBER: 1998250654 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9582276
TITLE: **Sphingosine kinase**-mediated Ca2+ signalling by G-protein-coupled receptors.
AUTHOR: Meyer zu Heringdorf D; Lass H; Alemany R; Laser K T; Neumann E; Zhang C; Schmidt M; Rauen U; Jakobs K H; van Koppen C J
CORPORATE SOURCE: Institut fur Pharmakologie, Universitat GH Essen, Essen, Germany.
SOURCE: EMBO journal, (1998 May 15) 17 (10) 2830-7.
Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980713
Last Updated on STN: 20000303
Entered Medline: 19980701

L13 ANSWER 99 OF 126 MEDLINE on STN
ACCESSION NUMBER: 1998240975 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9581819
TITLE: 1Alpha,25-dihydroxyvitamin D3 inhibits programmed cell death in HL-60 cells by activation of **sphingosine kinase**.
AUTHOR: Kleuser B; Cuvillier O; Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC 20007, USA.
CONTRACT NUMBER: CA61774 (NCI)
GM 43880 (NIGMS)
SOURCE: Cancer research, (1998 May 1) 58 (9) 1817-24.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980611
Last Updated on STN: 19980611
Entered Medline: 19980602

L13 ANSWER 100 OF 126 MEDLINE on STN
ACCESSION NUMBER: 1998211960 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9545263
TITLE: FcgammaRI coupling to phospholipase D initiates **sphingosine kinase**-mediated calcium mobilization and vesicular trafficking.
AUTHOR: Melendez A; Floto R A; Gillooly D J; Harnett M M; Allen J M
CORPORATE SOURCE: Department of Medicine and Therapeutics and Division of Biochemistry and Molecular Biology, University of Glasgow, Glasgow G12 8QQ, Scotland, United Kingdom.
SOURCE: Journal of biological chemistry, (1998 Apr 17) 273 (16) 9393-402.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980529
Last Updated on STN: 19980529
Entered Medline: 19980521

L13 ANSWER 101 OF 126 MEDLINE on STN
ACCESSION NUMBER: 1998193910 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9526097
TITLE: Roles of **sphingosine-1-phosphate** in cell growth, differentiation, and death.
AUTHOR: Spiegel S; Cuvillier O; Edsall L; Kohama T; Menzeleev R; Olivera A; Thomas D; Tu Z; Van Brocklyn J; Wang F
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC 20007,

USA.. spiegel@biochem1.basic-sci.georgetown.edu
CONTRACT NUMBER: RO1 CA61774 (NCI)
SOURCE: Biochemistry. Biokhimiia, (1998 Jan) 63 (1) 69-73. Ref: 47
Journal code: 0376536. ISSN: 0006-2979.
PUB. COUNTRY: RUSSIA: Russian Federation
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980507
Last Updated on STN: 19980507
Entered Medline: 19980428

L13 ANSWER 102 OF 126 MEDLINE on STN
ACCESSION NUMBER: 1998112841 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9446602
TITLE: **Sphingosine 1-phosphate** inhibits activation of caspases that cleave poly(ADP-ribose) polymerase and lamins during Fas- and ceramide-mediated apoptosis in Jurkat T lymphocytes.
AUTHOR: Cuvillier O; Rosenthal D S; Smulson M E; Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, District of Columbia 20007, USA.
CONTRACT NUMBER: CA61774 (NCI)
GM43880 (NIGMS)
SOURCE: Journal of biological chemistry, (1998 Jan 30) 273 (5) 2910-6.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980306
Last Updated on STN: 20021218
Entered Medline: 19980223

L13 ANSWER 103 OF 126 MEDLINE on STN
ACCESSION NUMBER: 97060474 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8903509
TITLE: Sphingolipid metabolism and cell growth regulation.
AUTHOR: Spiegel S; Merrill A H Jr
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, D.C. 20007, USA.
CONTRACT NUMBER: 1R01 CA61774 (NCI)
1R01 GM43880 (NIGMS)
1R01 GM46368 (NIGMS)
+
SOURCE: FASEB journal : official publication of the Federation of American Societies for Experimental Biology, (1996 Oct) 10 (12) 1388-97. Ref: 130
Journal code: 8804484. ISSN: 0892-6638.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128

Last Updated on STN: 19970128
Entered Medline: 19961203

L13 ANSWER 104 OF 126 MEDLINE on STN
ACCESSION NUMBER: 96267009 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8657285
TITLE: Suppression of ceramide-mediated programmed cell death by **sphingosine-1-phosphate**.
AUTHOR: Cuvillier O; Pirianov G; Kleuser B; Vanek P G; Coso O A; Gutkind S; Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC 20007, USA.
SOURCE: Nature, (1996 Jun 27) 381 (6585) 800-3.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 19960808
Last Updated on STN: 20000303
Entered Medline: 19960801

L13 ANSWER 105 OF 126 MEDLINE on STN
ACCESSION NUMBER: 96186814 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8602265
TITLE: Calcium mobilization via **sphingosine kinase** in signalling by the Fc epsilon RI antigen receptor.
AUTHOR: Choi O H; Kim J H; Kinet J P
CORPORATE SOURCE: Laboratory of Allergic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Rockville, Maryland 20852, USA.
SOURCE: Nature, (1996 Apr 18) 380 (6575) 634-6.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199605
ENTRY DATE: Entered STN: 19960517
Last Updated on STN: 19980206
Entered Medline: 19960508

L13 ANSWER 106 OF 126 MEDLINE on STN
ACCESSION NUMBER: 96140239 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8555236
TITLE: N,N-dimethylsphingosine inhibition of **sphingosine kinase** and **sphingosine 1-phosphate** activity in **human** platelets.
AUTHOR: Yatomi Y; Ruan F; Megidish T; Toyokuni T; Hakomori S; Igarashi Y
CORPORATE SOURCE: Biomembrane Institute, Seattle, Washington 98119, USA.
CONTRACT NUMBER: CA 42505 (NCI)
SOURCE: Biochemistry, (1996 Jan 16) 35 (2) 626-33.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 19960312

Last Updated on STN: 19960312
Entered Medline: 19960223

L13 ANSWER 107 OF 126 MEDLINE on STN
ACCESSION NUMBER: 95315536 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7795224
TITLE: **Sphingosine-1-phosphate**: a platelet-activating sphingolipid released from agonist-stimulated **human** platelets.
AUTHOR: Yatomi Y; Ruan F; Hakomori S; Igarashi Y
CORPORATE SOURCE: Biomembrane Institute, University of Washington, Seattle 98119, USA.
CONTRACT NUMBER: CA42505 (NCI)
SOURCE: Blood, (1995 Jul 1) 86 (1) 193-202.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950817
Last Updated on STN: 19950817
Entered Medline: 19950803

L13 ANSWER 108 OF 126 MEDLINE on STN
ACCESSION NUMBER: 94019798 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8413613
TITLE: **Sphingosine-1-phosphate** as second messenger in cell proliferation induced by PDGF and FCS mitogens.
AUTHOR: Olivera A; Spiegel S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC 20007.
SOURCE: Nature, (1993 Oct 7) 365 (6446) 557-60.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 20000303
Entered Medline: 19931109

L13 ANSWER 109 OF 126 MEDLINE on STN
ACCESSION NUMBER: 93392834 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8397478
TITLE: **Sphingosine kinase**: properties and cellular functions.
AUTHOR: Buehrer B M; Bell R M
CORPORATE SOURCE: Department of Biochemistry, Duke University Medical Center, Durham, North Carolina 27710.
SOURCE: Advances in lipid research, (1993) 26 59-67. Ref: 49
Journal code: 0000262. ISSN: 0065-2849.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199310
ENTRY DATE: Entered STN: 19931105
Last Updated on STN: 19931105

Entered Medline: 19931021

L13 ANSWER 110 OF 126 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2005215238 EMBASE
TITLE: **Sphingosine-1-phosphate** lyase regulates sensitivity of **human** cells to select chemotherapy drugs in a p38-dependent manner.
AUTHOR: Min J.; Van Veldhoven P.P.; Zhang L.; Hanigan M.H.; Alexander H.; Alexander S.
CORPORATE SOURCE: S. Alexander, Division of Biological Sciences, University of Missouri, 303 Tucker Hall, Columbia, MO 65211-7400, United States. alexanderst@missouri.edu
SOURCE: Molecular Cancer Research, (2005) Vol. 3, No. 5, pp. 287-296.
Refs: 35
ISSN: 1541-7786 CODEN: MCROC5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050602
Last Updated on STN: 20050602

L13 ANSWER 111 OF 126 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003269292 EMBASE
TITLE: Modulation of transforming growth factor-β (TGF-β) signaling by endogenous sphingolipid mediators.
AUTHOR: Sato M.; Markiewicz M.; Yamanaka M.; Bielawska A.; Mao C.; Obeid L.M.; Hannun Y.A.; Trojanowska M.
CORPORATE SOURCE: M. Trojanowska, Div. of Rheumatology and Immunology, Medical University of South Carolina, 96 Jonathan Lucas St., Charleston, SC 29425, United States. trojanme@musc.edu
SOURCE: Journal of Biological Chemistry, (14 Mar 2003) Vol. 278, No. 11, pp. 9276-9282.
Refs: 43
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20030731
Last Updated on STN: 20030731

L13 ANSWER 112 OF 126 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003137353 EMBASE
TITLE: Sphingolipids as therapeutics.
AUTHOR: Kester M.; Kolesnick R.
CORPORATE SOURCE: M. Kester, Department of Pharmacology, Penn Stt. Univ. College of Medicine, Hershey, PA, United States. mxk38@psu.edu
SOURCE: Pharmacological Research, (1 May 2003) Vol. 47, No. 5, pp. 365-371.
Refs: 83
ISSN: 1043-6618 CODEN: PHMREP
COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
016 Cancer
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20030417
Last Updated on STN: 20030417

L13 ANSWER 113 OF 126 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002382384 EMBASE
TITLE: **Sphingosine kinase**-dependent directional migration of leukocytes in response to phorbol ester.
AUTHOR: Kaneider N.C.; Djanani A.; Fischer-Colbrie R.; Wiedermann C.J.
CORPORATE SOURCE: C.J. Wiedermann, Department of Internal Medicine, Div. of General Internal Medicine, University of Innsbruck, Innsbruck, Austria. christian.wiedermann@uibk.ac.at
SOURCE: Biochemical and Biophysical Research Communications, (2002) Vol. 297, No. 4, pp. 806-810.
Refs: 24
ISSN: 0006-291X CODEN: BBRCA
PUBLISHER IDENT.: S 0006-291X(02)02304-5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20021114
Last Updated on STN: 20021114

L13 ANSWER 114 OF 126 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002066303 EMBASE
TITLE: Inhibition of recombinant **sphingosine kinases** by a novel inhibitors of microbial origin, F-12509A and B-5354c.
AUTHOR: Kono K.; Sugiura M.; Kohama T.
CORPORATE SOURCE: T. Kohama, Pharmacol./Mole. Biol. Research Lab., Research Institute, Sankyo Co. Ltd., 1-2-58 Hiromachi, Shinagawa, Tokyo 140-8710, Japan. kohama@shina.sankyo.co.jp
SOURCE: Journal of Antibiotics, (2002) Vol. 55, No. 1, pp. 99-103.
Refs: 27
ISSN: 0021-8820 CODEN: JANTAJ
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 20020301
Last Updated on STN: 20020301

L13 ANSWER 115 OF 126 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2000322129 EMBASE
TITLE: Overexpression of acid ceramidase protects from tumor necrosis factor-induced cell death.
AUTHOR: Strelow A.; Bernardo K.; Adam-Klages S.; Linke T.; Sandhoff

K.; Kronke M.; Adam D.
CORPORATE SOURCE: D. Adam, Institut fur Immunologie, Christian-Albrechts-University Kiel, Michaelisstr. 5, 24105 Kiel, Germany. dadam@email.uni-kiel.de
SOURCE: Journal of Experimental Medicine, (4 Sep 2000) Vol. 192, No. 5, pp. 601-611.
Refs: 43
ISSN: 0022-1007 CODEN: JEMEAV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000928
Last Updated on STN: 20000928

L13 ANSWER 116 OF 126 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 94238768 EMBASE
DOCUMENT NUMBER: 1994238768
TITLE: Sphingosine-mediated phosphatidylinositol metabolism and calcium mobilization.
AUTHOR: Chun Peng Chao; Lauledérkind S.J.F.; Ballou L.R.
CORPORATE SOURCE: Div. of Connective Tissue Diseases, Dept. of Medicine, University of Tennessee, 956 Court Ave.,Memphis, TN 38163, United States
SOURCE: Journal of Biological Chemistry, (1994) Vol. 269, No. 8, pp. 5849-5856.
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 940831
Last Updated on STN: 940831

L13 ANSWER 117 OF 126 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 92306563 EMBASE
DOCUMENT NUMBER: 1992306563
TITLE: Inhibition of **sphingosine kinase** in vitro and in platelets. Implications for signal transduction pathways.
AUTHOR: Buehrer B.M.; Bell R.M.
CORPORATE SOURCE: Department of Biochemistry, Duke University Medical Center,Durham, NC 27710, United States
SOURCE: Journal of Biological Chemistry, (1992) Vol. 267, No. 5, pp. 3154-3159.
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 921108
Last Updated on STN: 921108

L13 ANSWER 118 OF 126 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2002-06038 BIOTECHDS
TITLE: Novel **sphingosine kinase** variants which

exhibit reduced catalytic activity useful for modulating cellular functional activity and treating or preventing inflammatory, degenerative diseases and neoplastic conditions

mutant **sphingosine-kinase** produced by site-directed mutagenesis useful for gene therapy and prophylaxis

AUTHOR: PITSON S; MORETTI P; ZEBOL J; XIA P; GAMBLE J; VADAS M; D'ANDREA R; WATTENBERG B
PATENT ASSIGNEE: MEDVET SCI PTY LTD
PATENT INFO: WO 2002000887 3 Jan 2002
APPLICATION INFO: WO 2000-AU730 28 Jun 2000
PRIORITY INFO: AU 2001-2749 29 Jan 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-130896 [17]

L13 ANSWER 119 OF 126 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:4884 SCISEARCH
THE GENUINE ARTICLE: 878TT
TITLE: Synthesis of 7-oxasphingosine and -ceramide **analogues** and their evaluation in a model for apoptosis
AUTHOR: Rajan R; Wallimann K; Vasella A (Reprint); Pace D; Genazzani A A; Canonico P L; Condorelli F
CORPORATE SOURCE: ETH Honggerberg, Organ Chem Lab, Wolfgang Pauli Str 10, CH-8093 Zurich, Switzerland (Reprint); ETH Honggerberg, Organ Chem Lab, CH-8093 Zurich, Switzerland; Univ Piemonte Orientale, DISCAFF, I-28100 Novara, Italy
COUNTRY OF AUTHOR: Switzerland; Italy
SOURCE: CHEMISTRY & BIODIVERSITY, (1 DEC 2004) Vol. 1, No. 11, pp. 1785-1799.
Publisher: VERLAG HELVETICA CHIMICA ACTA AG, HOFWIESENSTRASSE 26, POSTFACH, CH-8042 ZURICH, SWITZERLAND.
ISSN: 1612-1872.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 35
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L13 ANSWER 120 OF 126 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:252481 SCISEARCH
THE GENUINE ARTICLE: 532JF
TITLE: 1-O-Hexadecyl-2-desoxy-2-amino-sn-glycerol, a substrate for **human sphingosine kinase**
AUTHOR: Gijsbers S; Asselberghs S; Herdewijn P; Van Veldhoven P P (Reprint)
CORPORATE SOURCE: Katholieke Univ Leuven, Fac Geneeskunde, Dept Mol Celbiol, Afdeling Farmakol, Campus Gasthuisberg, B-3000 Louvain, Belgium (Reprint); Katholieke Univ Leuven, Fac Geneeskunde, Dept Mol Celbiol, Afdeling Farmakol, B-3000 Louvain, Belgium; Catholic Univ Louvain, Rega Inst Med Res, Fac Farmaceut Wetenschappen, B-3000 Louvain, Belgium
COUNTRY OF AUTHOR: Belgium
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA-MOLECULAR AND CELL BIOLOGY OF LIPIDS, (30 JAN 2002) Vol. 1580, No. 1, pp. 1-8.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 1388-1981.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English

REFERENCE COUNT: 29
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L13 ANSWER 121 OF 126 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:451328 SCISEARCH
THE GENUINE ARTICLE: 436RH
TITLE: S-15183a and b, new **sphingosine kinase** inhibitors, produced by a fungus
AUTHOR: Kono K; Tanaka M; Ono Y; Hosoya T; Ogita T; Kohama T (Reprint)
CORPORATE SOURCE: Sankyo Co Ltd, Inst Res, Pharmacol & Mol Biol Res Labs, 1-2-58 Hiromachi, Tokyo 1408710, Japan (Reprint); Sankyo Co Ltd, Inst Res, Pharmacol & Mol Biol Res Labs, Tokyo 1408710, Japan; Sankyo Co Ltd, Inst Res, Exploratory Chem Res Labs, Tokyo 1408710, Japan; Sankyo Co Ltd, Inst Res, Lead Discovery Res Labs, Tokyo 1408710, Japan; Sankyo Co Ltd, Inst Res, Drug Metab & Pharmacokinet Res Labs, Tokyo 1408710, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: JOURNAL OF ANTIBIOTICS, (MAY 2001) Vol. 54, No. 5, pp. 415-420.
Publisher: JAPAN ANTIBIOT RES ASSN, 2 20 8 KAMIOSAKI SHINAGAWA KU, TOKYO, 141, JAPAN.
ISSN: 0021-8820.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 30
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L13 ANSWER 122 OF 126 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:931154 HCAPLUS
DOCUMENT NUMBER: 140:714
TITLE: Use of **sphingosine-1-phosphate** (S1P) receptor agonists for the treatment of cancer
INVENTOR(S): Baumruker, Thomas; Brinkmann, Volker; La Montagne, Kenneth Richard; Lassota, Peter T.; Mechtcheriakova, Diana; Wood, Jeanette Marjorie
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma GMBH
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097028	A1	20031127	WO 2003-EP5125	20030515
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2483594	AA	20031127	CA 2003-2483594	20030515
EP 1505959	A1	20050216	EP 2003-730049	20030515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003011173	A	20050315	BR 2003-11173	20030515

PRIORITY APPLN. INFO.:

GB 2002-11261	A	20020516
US 2002-390411P	P	20020620
GB 2002-17150	A	20020724
US 2003-449739P	P	20030224
WO 2003-EP5125	W	20030515

OTHER SOURCE(S): MARPAT 140:714
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 123 OF 126 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:796515 HCAPLUS
DOCUMENT NUMBER: 139:303797
TITLE: Variants of mammalian **sphingosine kinase** with reduced catalytic activity and their use in controlling **sphingosine-1-phosphate** activated processes
INVENTOR(S): Pitson, Stuart M.; Xia, Pu; Moretti, Paul A.; Verwey, Julia R.; Vadas, Mathew A.; Wattenberg, Brian W.
PATENT ASSIGNEE(S): Medvet Science Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082322	A1	20031009	WO 2003-AU388	20030328
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2480661	AA	20031009	CA 2003-2480661	20030328
EP 1499343	A1	20050126	EP 2003-745226	20030328
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:

AU 2002-1448	A	20020328
AU 2002-1538	A	20020405
AU 2002-1621	A	20020408
AU 2002-951668	A	20020919
AU 2003-900230	A	20030121
WO 2003-AU388	W	20030328

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 124 OF 126 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:737283 HCAPLUS
DOCUMENT NUMBER: 139:257275
TITLE: Cloning of cDNAs for **sphingosine-1-phosphate** lyases and **sphingosine kinases** from **human** and Drosophila, and their use for modulation of sphingolipid metabolism and/or signaling in cancer diagnosis and therapy
INVENTOR(S): Saba, Julie D.; Fyrst, Henrik
PATENT ASSIGNEE(S): Children's Hospital Oakland Research Institute, USA
SOURCE: U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of

U.S.Ser. No.356,643.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003175939	A1	20030918	US 2002-53510	20020117
US 6830881	B2	20041214		
US 6423527	B1	20020723	US 1997-939309	19970929
US 6569666	B1	20030527	US 1999-356643	19990719
US 2003059922	A1	20030327	US 2002-286175	20021030
CA 2473680	AA	20030731	CA 2003-2473680	20030117
WO 2003062390	A2	20030731	WO 2003-US1739	20030117
WO 2003062390	A3	20050203		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1517989	A2	20050330	EP 2003-732010	20030117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004126834	A1	20040701	US 2003-622011	20030716

PRIORITY APPLN. INFO.:

US 1997-939309	A2	19970929
US 1999-356643	A2	19990719
US 2001-849180	A1	20010504
US 2002-349582P	P	20020117
US 2002-53510	A	20020117
US 2003-348052	A2	20030117
WO 2003-US1739	W	20030117

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 125 OF 126 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:504646 HCAPLUS
DOCUMENT NUMBER: 137:83610
TITLE: Compositions and methods for the treatment and prevention of cardiovascular diseases and disorders, and for identifying agents therapeutic therefor
INVENTOR(S): Sabbadini, Roger A.
PATENT ASSIGNEE(S): Medlyte, Inc., USA
SOURCE: PCT Int. Appl., 188 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002051439	A2	20020704	WO 2001-US50785	20011221
WO 2002051439	A3	20030814		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

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            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
            UG, US, UZ, VN, YU, ZA, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
            GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
            GN, GQ, GW, ML, MR, NE, SN, TD, TG
    CA 2432978          AA    20020704    CA 2001-2432978        20011221
    US 2003026799       A1    20030206    US 2001-28156          20011221
    US 6881546          B2    20050419
    US 2003027304       A1    20030206    US 2001-29401          20011221
    US 6858383          B2    20050222
    US 2003096022       A1    20030522    US 2001-29372          20011221
    EP 1363643          A2    20031126    EP 2001-987517         20011221
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
    US 2004247603       A1    20041209    US 2004-820582         20040407
PRIORITY APPLN. INFO.:                      US 2000-257926P     P  20001222
                                            US 2001-28156       A3 20011221
                                            WO 2001-US50785     W  20011221
OTHER SOURCE(S):        MARPAT 137:83610

L13  ANSWER 126 OF 126  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:       2002:271073  HCAPLUS
DOCUMENT NUMBER:        136:289050
TITLE:                  Using ceramide-generating retinoids in combination
                        with other drugs for treatment of hyperproliferative
                        cancer disorders
INVENTOR(S):            Maurer, Barry J.; Reynolds, C. Patrick
PATENT ASSIGNEE(S):     Children's Hospital, USA
SOURCE:                 U.S., 31 pp., Cont.-in-part of U.S. Ser. No. 342,019.
                        CODEN: USXXAM
DOCUMENT TYPE:          Patent
LANGUAGE:               English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

    PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
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    US 6368831          B1     20020409    US 1999-471944          19991223
    US 6352844          B1     20020305    US 1999-342019          19990628
    WO 2001047513       A1     20010705    WO 2000-US29996         20001031
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
            HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
            LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
            SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
            YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
            DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
            CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
    EP 1239851          A1     20020918    EP 2000-975519          20001031
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL
PRIORITY APPLN. INFO.:                      US 1998-91138P      P  19980629
                                            US 1999-342019      A2 19990628
                                            US 1999-471944      A  19991223
                                            WO 2000-US29996     W  20001031
REFERENCE COUNT:        24    THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS
                              RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d his
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     (FILE 'HOME' ENTERED AT 10:16:41 ON 23 JUN 2005)

     FILE 'STNGUIDE' ENTERED AT 10:16:54 ON 23 JUN 2005

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 10:17:40 ON 23 JUN 2005
L1         22912 S SPHINGOSINE
L2          1950 S L1 (W)KINASE?
L3           104 S HUMAN (W)L2
L4            54 DUP REM L3 (50 DUPLICATES REMOVED)
L5       7132348 S CLON? OR EXPRESS? OR RECOMBINANT
L6            36 S L4 AND L5
L7       3507345 S MIMETIC? OR DERIVATIVE? OR ANALOGUE?
L8           388 S L2 AND L7
L9          6947 S SPHINGOSINE-1-PHOSPHATE
L10          320 S L8 AND L9
L11          320 S L10 AND KINASE?
L12          211 DUP REM L11 (109 DUPLICATES REMOVED)
L13          126 S HUMAN AND L12

=> e pitson s m/au
E1             4     PITSON L C/AU
E2            20     PITSON S/AU
E3            94 --> PITSON S M/AU
E4             1     PITSON SM/AU
E5             8     PITSON STUART/AU
E6            66     PITSON STUART M/AU
E7             1     PITSON STUART MAXWELL/AU
E8             3     PITSOPOULOS C N/AU
E9            14     PITSOS M A/AU
E10            3     PITSOS N/AU
E11            1     PITSOTSKII B I/AU
E12           25     PITSOULAKIS G/AU

=> s e3-e7
L14          170 ("PITSON S M"/AU OR "PITSON SM"/AU OR "PITSON STUART"/AU OR
                 "PITSON STUART M"/AU OR "PITSON STUART MAXWELL"/AU)

=> e wattenberg b w/au
E1            23     WATTENBERG B/AU
E2             1     WATTENBERG B J/AU
E3           118 --> WATTENBERG B W/AU
E4             1     WATTENBERG BILL/AU
E5             4     WATTENBERG BINKS/AU
E6            45     WATTENBERG BINKS W/AU
E7             3     WATTENBERG BRIAN/AU
E8             1     WATTENBERG BRIAN W/AU
E9             2     WATTENBERG BRIAN WOLFF/AU
E10           12     WATTENBERG C A/AU
E11            2     WATTENBERG CARL A/AU
E12            4     WATTENBERG D/AU

=> s e3-e9
L15          174 ("WATTENBERG B W"/AU OR "WATTENBERG BILL"/AU OR "WATTENBERG
                 BINKS"/AU OR "WATTENBERG BINKS W"/AU OR "WATTENBERG BRIAN"/AU
                 OR "WATTENBERG BRIAN W"/AU OR "WATTENBERG BRIAN WOLFF"/AU)

=> e diandrea r j/au
E1             1     DIANDERAS DE ACOSTA VILMA/AU
E2             3     DIANDERAS M T/AU
E3             0 --> DIANDREA R J/AU
E4             1     DIANDRETH ANITA NAVRATIL/AU
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E5          12      DIANDRETH J R/AU
E6           1      DIANDRETH JAMES RICHARD/AU
E7           1      DIANDRETH M/AU
E8           2      DIANDRIOLE E T/AU
E9           2      DIANE/AU
E10          1      DIANE A/AU
E11          3      DIANE ABDOULAYE/AU
E12          5      DIANE B/AU

=> e d'Andrea r j/au
MISMATCHED QUOTE IN EXPAND TERM
MISMATCHED QUOTE IN EXPAND TERM
MISMATCHED QUOTE IN EXPAND TERM
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MISMATCHED QUOTE IN EXPAND TERM
Quotation marks (or apostrophes) must be used in pairs,
one before and one after the expression you are setting
off or masking.

=> e gamble j r/au
E1           9      GAMBLE J N/AU
E2           1      GAMBLE J Q/AU
E3         355 --> GAMBLE J R/AU
E4           1      GAMBLE J R */AU
E5           7      GAMBLE J R JR/AU
E6           2      GAMBLE J S/AU
E7          26      GAMBLE J T/AU
E8          45      GAMBLE J W/AU
E9           2      GAMBLE JACKIE/AU
E10         21      GAMBLE JAMES/AU
E11         16      GAMBLE JAMES G/AU
E12         22      GAMBLE JAMES L/AU

=> s e3
L16        355 "GAMBLE J R"/AU

=> e vadas m a/au
E1           1      VADAS LUCIEN/AU
E2         114      VADAS M/AU
E3        1005 --> VADAS M A/AU
E4           1      VADAS M A */AU
E5           2      VADAS MA/AU
E6          36      VADAS MATHEW/AU
E7         212      VADAS MATHEW A/AU
E8          16      VADAS MATHEW ALEXANDER/AU
E9          10      VADAS MATTHEW/AU
E10         13      VADAS MATTHEW A/AU
E11          5      VADAS O/AU
E12        420      VADAS P/AU

=> s e3-e8
L17       1272 ("VADAS M A"/AU OR "VADAS M A *"/AU OR "VADAS MA"/AU OR "VADAS
               MATHEW"/AU OR "VADAS MATHEW A"/AU OR "VADAS MATHEW ALEXANDER"/AU
               )

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     (FILE 'HOME' ENTERED AT 10:16:41 ON 23 JUN 2005)

     FILE 'STNGUIDE' ENTERED AT 10:16:54 ON 23 JUN 2005
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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 10:17:40 ON 23 JUN 2005
L1         22912 S SPHINGOSINE
L2          1950 S L1 (W)KINASE?
L3           104 S HUMAN (W)L2
L4            54 DUP REM L3 (50 DUPLICATES REMOVED)
L5       7132348 S CLON? OR EXPRESS? OR RECOMBINANT
L6            36 S L4 AND L5
L7       3507345 S MIMETIC? OR DERIVATIVE? OR ANALOGUE?
L8           388 S L2 AND L7
L9          6947 S SPHINGOSINE-1-PHOSPHATE
L10          320 S L8 AND L9
L11          320 S L10 AND KINASE?
L12          211 DUP REM L11 (109 DUPLICATES REMOVED)
L13          126 S HUMAN AND L12
                 E PITSON S M/AU
L14          170 S E3-E7
                 E WATTENBERG B W/AU
L15          174 S E3-E9
                 E DIANDREA R J/AU
                 E GAMBLE J R/AU
L16          355 S E3
                 E VADAS M A/AU
L17         1272 S E3-E8

=> s l14 or l15 or l16 or l17
L18        1564 L14 OR L15 OR L16 OR L17

=> s l2 and l18
L19         109 L2 AND L18

=> dup rem l19
PROCESSING COMPLETED FOR L19
L20           33 DUP REM L19 (76 DUPLICATES REMOVED)

=> d 1-33 ibib ab

L20 ANSWER 1 OF 33  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:36538  HCAPLUS
DOCUMENT NUMBER:          142:107384
TITLE:                    Method of modulating cell growth by modulating
                          sphingosine kinase for treatment of
                          cancer and useful agents
INVENTOR(S):              Vadas, Mathew; Gamble, Jennifer; Xia, Pu;
                          Wang, Lijun; Sukocheva, Olga
PATENT ASSIGNEE(S):       Medvet Science Pty Ltd., Australia
SOURCE:                   U.S. Pat. Appl. Publ., 35 pp., Cont.-in-part of U.S.
                          Ser. No. 275,686.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
     ---------------     ----   --------    --------------------     --------
     US 2005009732        A1    20050113    US 2004-780897           20040219
     US 2004014635        A1    20040122    US 2003-275686           20030625
PRIORITY APPLN. INFO.:                      AU 2003-900729      A    20030219
                                            US 2003-447707P     P    20030219
                                            US 2003-275686      A2   20030625
                                            AU 2000-7447        A    20000511
```

WO 2001-AU539 W 20010511

AB A method of modulating the growth of a cell, such as a neoplastic or malignant cell from the colon, stomach, lung, brain, bone, esophagus, pancreas, breast, ovary or uterus includes contacting the cell with an agent for a time and under conditions sufficient to modulate the functional activity of **sphingosine kinase** in which down-regulation of the functional activity of the **sphingosine kinase** down-regulates growth of the cells and up-regulation of the functional activity of this **sphingosine kinase** up-regulates the growth of the cell. The down-regulation can reduce the functional activity of this **sphingosine kinase** to an oncogenic ineffective level. Agents useful in the invention include N,N-dimethylspingosine and DL-threo-dihydrosphingosine. A correlation between cell growth, in particular oncogenesis, and modulation in the level of activity of **sphingosine kinase** was determined for 3T3 fibroblasts and for MCF-7 breast cancer cells. Mice injected with 3T3 cells overexpressing **sphingosine kinase** developed tumors within 3 to 4 wk.

L20 ANSWER 2 OF 33 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2005119304 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15749892
TITLE: **Sphingosine kinase** 1 (SK1) is recruited to nascent phagosomes in human macrophages: inhibition of SK1 translocation by Mycobacterium tuberculosis.
AUTHOR: Thompson Christopher R; Iyer Shankar S; Melrose Natalie; VanOosten Rebecca; Johnson Korey; **Pitson Stuart M** ; Obeid Lina M; Kusner David J
CORPORATE SOURCE: Inflammation Program, University of Iowa Carver College of Medicine, Coralville, IA 52241, USA.
CONTRACT NUMBER: R01 AI055916 (NIAID)
R01 GM062887 (NIGMS)
R01 GM62302 (NIGMS)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2005 Mar 15) 174 (6) 3551-61.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 20050308
Last Updated on STN: 20050429
Entered Medline: 20050428

AB Mycobacterium tuberculosis (M.tb) is a leading cause of global infectious mortality. The pathogenesis of tuberculosis involves inhibition of phagosome maturation, leading to survival of M.tb within human macrophages. A key determinant is M.tb-induced inhibition of macrophage **sphingosine kinase** (SK) activity, which normally induces Ca2+ signaling and phagosome maturation. Our objective was to determine the spatial localization of SK during phagocytosis and its inhibition by M.tb. Stimulation of SK activity by killed M.tb, live Staphylococcus aureus, or latex beads was associated with translocation of cytosolic SK1 to the phagosome membrane. In contrast, SK1 did not associate with phagosomes containing live M.tb. To characterize the mechanism of phagosomal translocation, live cell confocal microscopy was used to compare the localization of wild-type SK1, catalytically inactive SK1G82D, and a phosphorylation-defective mutant that does not undergo plasma membrane translocation (SK1S225A). The magnitude and kinetics of translocation of SK1G82D and SK1S225A to latex bead phagosomes were indistinguishable from those of wild-type SK1, indicating that novel determinants regulate the association of SK1 with nascent phagosomes. These data are consistent with a model in which M.tb inhibits both the

activation and phagosomal translocation of SK1 to block the localized Ca2+ transients required for phagosome maturation.

L20 ANSWER 3 OF 33 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005170340 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15632208
TITLE: **Sphingosine kinase**-1 enhances endothelial cell survival through a PECAM-1-dependent activation of PI-3K/Akt and regulation of Bcl-2 family members.
AUTHOR: Limaye Vidya; Li Xiaochun; Hahn Chris; Xia Pu; Berndt Michael C; **Vadas Mathew A**; Gamble Jennifer R
CORPORATE SOURCE: Hanson Institute, Institute of Medical and Veterinary Science, Adelaide, SA, Australia.
SOURCE: Blood, (2005 Apr 15) 105 (8) 3169-77. Electronic Publication: 2005-01-04.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200505
ENTRY DATE: Entered STN: 20050402
Last Updated on STN: 20050514
Entered Medline: 20050513

AB Sphingosine-1-phosphate (S1P), the bioactive product of **sphingosine kinase** (SK) activation, is a survival factor for endothelial cells. The mechanism of SK-mediated survival was investigated in endothelial cells with moderately raised intracellular SK activity. Overexpression of SK mediated survival primarily through the activation of the phosphatidyl inositol 3-kinase (PI-3K)/protein kinase B (Akt/PKB) pathway and an associated up-regulation of the antiapoptotic protein B cell lymphoma gene 2 (Bcl-2) and down-regulation of the proapoptotic protein bisindolylmaleimide (Bcl-2 interacting mediator of cell death; Bim). In addition there was an up-regulation and dephosphorylation of the junctional molecule platelet endothelial cell adhesion molecule-1 (PECAM-1), which was obligatory for activation of the PI-3K/Akt pathway, for SK-induced cell survival, and for the changes in the apoptosis-related proteins. Thus, raised intracellular SK activity induced a molecule involved in cell-cell interactions to augment cell survival through a PI-3K/Akt-dependent pathway. This is distinct from the activation of both PI-3K/Akt and mitogen-activated protein kinase (MAPK) pathways seen with exogenously added S1P. Cells overexpressing SK showed enhanced survival under conditions of serum deprivation and absence of attachment to extracellular matrix, suggesting a role for SK in the regulation of vascular phenomena that occur under conditions of stress, such as angiogenesis and survival in unattached states, as would be required for a circulating endothelial cell.

L20 ANSWER 4 OF 33 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2005132026 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15763425
TITLE: Enhancement of intracellular sphingosine-1-phosphate production by inositol 1,4,5-trisphosphate-evoked calcium mobilisation in HEK-293 cells: endogenous sphingosine-1-phosphate as a modulator of the calcium response.
AUTHOR: Blom Tomas; Slotte J Peter; **Pitson Stuart M**; Tornquist Kid
CORPORATE SOURCE: Department of Biology, Abo Akademi University, BioCity, Artillerigatan 6, 20520 Turku, Finland.
SOURCE: Cellular signalling, (2005 Jul) 17 (7) 827-36. Electronic Publication: 2005-01-07.

Journal code: 8904683. ISSN: 0898-6568.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20050315
Last Updated on STN: 20050423

AB Sphingosine-1-phosphate (S1P) regulates many cellular functions, such as migration, differentiation and growth. The effects of S1P are thought to be primarily mediated by G-protein coupled receptors, but an intracellular function as a calcium releasing second messenger has also been proposed. Here we show that in HEK-293 cells, exogenous S1P mobilises sequestered calcium by a mechanism primarily dependent on the phospholipase C (PLC)/inositol 1,4,5-trisphosphate (IP3) pathway, and secondarily on the subsequent synthesis of intracellular S1P. Stimulating HEK-293 cells exogenously with S1P increased the production of both inositol phosphates and intracellular S1P. The calcium response was inhibited in cells treated with 2-APB, caffeine or U73122, showing that the PLC/IP3 pathway for calcium release is activated in response to exogenous S1P. The calcium response was partially inhibited in cells treated with the **sphingosine kinase** inhibitor DMS and in cells expressing a catalytically inactive **sphingosine kinase**, showing that endogenously produced S1P is also involved. Importantly, 2-APB and U73122 inhibited the S1P-evoked production of intracellular S1P. S1P is therefore not likely a major calcium releasing second messenger in HEK-293 cells, but rather a secondary regulator of calcium mobilisation.

L20 ANSWER 5 OF 33 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2005004399 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15623571
TITLE: Phosphorylation-dependent translocation of **sphingosine kinase** to the plasma membrane drives its oncogenic signalling.
AUTHOR: **Pitson Stuart M**; Xia Pu; Leclercq Tamara M; Moretti Paul A B; Zebol Julia R; Lynn Helen E; **Wattenberg Binks W; Vadas Mathew A**
CORPORATE SOURCE: Hanson Institute and Division of Human Immunology, Institute of Medical and Veterinary Science, Adelaide SA 5000, Australia.. stuart.pitson@imvs.sa.gov.au
SOURCE: Journal of experimental medicine, (2005 Jan 3) 201 (1) 49-54. Electronic Publication: 2004-12-28..
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 20050105
Last Updated on STN: 20050329
Entered Medline: 20050328

AB **Sphingosine kinase** (SK) 1 catalyzes the formation of the bioactive lipid sphingosine 1-phosphate, and has been implicated in several biological processes in mammalian cells, including enhanced proliferation, inhibition of apoptosis, and oncogenesis. Human SK (hSK) 1 possesses high instrinsic catalytic activity which can be further increased by a diverse array of cellular agonists. We have shown previously that this activation occurs as a direct consequence of extracellular signal-regulated kinase 1/2-mediated phosphorylation at Ser225, which not only increases catalytic activity, but is also necessary for agonist-induced translocation of hSK1 to the plasma membrane. In this study, we report that the oncogenic effects of overexpressed hSK1 are blocked by mutation of the phosphorylation site despite the phosphorylation-deficient form of the enzyme retaining full instrinsic

catalytic activity. This indicates that oncogenic signaling by hSK1 relies on a phosphorylation-dependent function beyond increasing enzyme activity. We demonstrate, through constitutive localization of the phosphorylation-deficient form of hSK1 to the plasma membrane, that hSK1 translocation is the key effect of phosphorylation in oncogenic signaling by this enzyme. Thus, phosphorylation of hSK1 is essential for oncogenic signaling, and is brought about through phosphorylation-induced translocation of hSK1 to the plasma membrane, rather than from enhanced catalytic activity of this enzyme.

L20 ANSWER 6 OF 33 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
DUPLICATE 5
ACCESSION NUMBER: 2004-14417 BIOTECHDS
TITLE: Modulating mammalian endothelial cell functional characteristics such as viability, proliferation and differentiation, useful for treating tumor, rheumatoid arthritis, involves modulating functional level of **sphingosine kinase**;
useful for preparation of a medicament for gene therapy
AUTHOR: **GAMBLE J R**; VADAS M; PITSON S; XIA P; LIMAYE V
PATENT ASSIGNEE: MEDVET SCI PTY LTD
PATENT INFO: WO 2004035786 29 Apr 2004
APPLICATION INFO: WO 2003-AU1356 14 Oct 2003
PRIORITY INFO: AU 2003-902047 30 Apr 2003; AU 2002-952032 14 Oct 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-365161 [34]
AB DERWENT ABSTRACT:
NOVELTY - Modulating (M1) one or more mammalian endothelial cell functional characteristics, involves modulating the functional level of **sphingosine kinase**, where inducing over-expression of the **sphingosine kinase** level modulates one or more of the functional characteristics of the endothelial cell.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) use of an agent capable of modulating the functional level of **sphingosine kinase** in the manufacture of a medicament for (M1); (2) use of **sphingosine kinase** or a nucleic acid encoding **sphingosine kinase** in the manufacture of a medicament for (M1); and (3) a pharmaceutical composition comprising modulatory agent and one or more carriers and/or diluents when used in (M1).

WIDER DISCLOSURE - The following are disclosed: (1) generating endothelial cells by (M1); and (2) endothelial cells generated by (M1).

BIOTECHNOLOGY - Preferred Method: In (M1), the endothelial cell is a vascular endothelial cell. The endothelial cell functional characteristic is up-regulatable by **sphingosine kinase** over-expression and the characteristic is one or more of viability, proliferation, differentiation, cell surface molecule expression, cytokine responsiveness or enhanced proliferation or viability. The cell surface molecule is an adhesion molecule. The functional characteristic is up-regulated. The endothelial cell functional characteristic is up-regulatable by **sphingosine kinase** over-expression and the characteristic is the induction of a pro-inflammatory phenotype or angiogenic phenotype or maintenance of the CD34+ endothelial cell progenitor phenotype. The pro-inflammatory phenotype is down-regulated. The angiogenic phenotype is up-regulated or down-regulated. The CD34+ progenitor phenotype is maintained. The modulation is up-regulation of **sphingosine kinase** levels and the up-regulation is achieved by introducing into the endothelial cell a nucleic acid molecule encoding **sphingosine kinase** or its functional equivalent, derivative or homologue or the **sphingosine kinase** expression product or its functional derivative, homologue, analogue, equivalent or mimetic. The modulation is achieved by

contacting the endothelial cell with a proteinaceous or non-proteinaceous molecule which modulates transcriptional and/or translational regulation of the **sphingosine kinase** gene. Modulation is up-regulation of **sphingosine kinase** levels and the up-regulation is achieved by contacting the endothelial cell with a proteinaceous or non-proteinaceous molecule, which functions as an agonist of the **sphingosine kinase** expression product. The modulation is down-regulation of **sphingosine kinase** levels and the down-regulation is achieved by contacting the endothelial cell with a proteinaceous or non-proteinaceous molecule which functions as an antagonist to the **sphingosine kinase** expression product. The molecule is a mutant **sphingosine kinase** which mutant is characterized by substitution of the glycine residue at position 82 to aspartate. The endothelial cell activity is modulated in vivo or in vitro. In the method of using an agent capable of modulating **sphingosine kinase** in the manufacture of medicament, the agent is a proteinaceous or non-proteinaceous molecule, which modulates transcriptional and/or translational regulation of the **sphingosine kinase** gene, functions as an agonist of **sphingosine kinase** activity or functions as an antagonist of **sphingosine kinase** activity.

ACTIVITY - Vulnerary; Antiarthritic; Antirheumatic; Cytostatic; Antiangiogenic. No biological data given.

MECHANISM OF ACTION - Protein Kinase Modulator; **Sphingosine Kinases** Modulator; Gene Therapy. Adenovirus carrying the **sphingosine kinase** (SK) gene were used to transfect vascular endothelial cells. Overexpression of SK was measured and found to be increased by 5.17-fold. Use of DAPI stain under basal conditions and under serum deprivation conditions showed that cells overexpressing SK were less likely to undergo apoptosis. Caspase-3 activity was also measured and found to be suppressed under higher SK levels.

USE - For modulating mammalian endothelial cell functions such as viability, proliferation, differentiation, cell surface molecule expression, cytokine responsiveness or enhanced proliferation or viability. (M1) is also useful for prophylaxis and/or treatment of a condition characterized by aberrant or otherwise unwanted endothelial cell functioning in a mammal. The medicament manufactured using agent capable of modulating the functional level of **sphingosine kinase** or a nucleic acid encoding **sphingosine kinase**, is useful for treating a condition characterized by aberrant or otherwise unwanted endothelial cell functioning in a mammal. The condition is vascular engraftment, wound repair, tissue or organ transplantation or the repair of devascularised tissue and the modulated endothelial cell functional characteristic is one or more of enhanced endothelial cell proliferation, enhanced endothelial cell viability or maintenance of the CD34+ progenitor phenotype. The condition is an inflammatory condition and the modulated endothelial cell functional characteristic is down-regulation of one or more of an endothelial cell inflammatory of angiogenic phenotype. The condition is rheumatoid arthritis. The condition is characterized by unwanted angiogenesis and the modulated endothelial cell functional characteristic is down-regulation of an endothelial cell angiogenic phenotype. The condition is a tumor (all claimed).

ADMINISTRATION - Administration of the modulatory agent is by oral, intravenous, intramuscular, intraperitoneal, subcutaneous, intradermal, suppository routes or implanting (e.g., using slow release molecules) at 0.1-1 mg/kg body weight/day.

EXAMPLE - To determine the effect on endothelial cell function of over-expression of **sphingosine kinase** (SK), HUVEC (human vascular endothelial cells) were infected with either retrovirus containing SK or adenovirus containing SK, at 1 plate forming units (pfu)/cell. This level of adenovirus infection was chosen since it resulted in similar levels of SK activity as tumor necrosis factor (TNF)

alpha-stimulation of endogenous SK in endothelial cells, and similar levels of SK activity as was achieved with retrovirus-mediated gene delivery. To determine whether over-expression of SK results in changes to the endogenous phenotype of endothelial cells, the adhesion molecule expression was investigated on these infected cells. Retrovirus-mediated over-expression of SK up-regulated basal VCAM-1 expression. Adenoviral-mediated over-expression of SK resulted in a similar increase in VCAM-1 expression. In contrast to VCAM-1, basal E selectin expression was not altered in cells over-expressing SK generated by retroviral or adenoviral-mediated transfection. As over-expression of SK induced basal levels of VCAM-1. To determine whether these cells exhibited an altered response to stimulation with TNFalpha-induced up-regulation of VCAM-1 expression. Interestingly, cells over-expressing SK also showed an enhanced E Selectin response following stimulation with TNFalpha even though basal E Selectin expression was not altered. Over-expression of dominant-negative SK (G82D) significantly inhibited the induction of VCAM-1 and E Selectin in response to TNFalpha compared with empty vector (EV). Significant levels of both adhesion molecules were induced in cells over-expressing SK. Retroviral and adenoviral delivery of SK generated similar phenotypes in endothelial cells, that of enhanced expression of adhesion molecules and altered response to TNFalpha. However the adenoviral system enabled large number of cells to be rapidly generated. To determine whether the alteration in adhesion molecule expression resulting from intracellular over-expression of SK had functional consequences, neutrophil adhesion to endothelial cells was measured. In the basal state, cells over-expressing SK showed significant neutrophil adhesion, in contrast to control cells which did not bind neutrophils. Stimulation of endothelial cells with a low dose of TNFalpha (0.04 ng/ml) resulted in minimal neutrophil adhesion in control cells, but significantly greater adhesion to cells over-expressing SK. Consistent with a role for SK in mediating PMN adhesion, endothelial cells over-expressing the dominant-negative SK, G82D, inhibited PMN adhesion in response to stimulation with TNF alpha. To determine whether SK over-expression also enhances the ability of endothelial cells to form tubes. Endothelial cells were plated onto the complex basement membrane matrix, Matrigel, Equivalent numbers of cells over-expressing SK and EV were seeded, cells over-expressing SK had already commenced realignment whereas the EV cells remained disorganized. By 30 minutes cells over-expressing SK showed greater evidence of tube alignment compared with EV cells. By one hour tube formation by cells over-expressing SK was highly developed compared with EV cells. By 18 hours, a time where tube formation was complete, both cells over-expressing SK and EV cells showed a similar pattern of tube formation. These results suggest that over-expression of SK stimulates the rate of tube formation. (91 pages)

L20 ANSWER 7 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:802879 HCAPLUS
DOCUMENT NUMBER: 141:293029
TITLE: Modulating smooth muscle cell functioning by modulating **sphingosine kinase** mediated signalling
INVENTOR(S): **Pitson, Stuart M.**; Bolz, Steffen-Sebastian
PATENT ASSIGNEE(S): Medvet Science Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004083453	A1	20040930	WO 2004-AU336	20040318

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AU 2003-901270 A 20030318

AB The present invention relates generally to a method of modulating smooth muscle cell functioning and agents useful for same. More particularly, the present invention relates to a method of modulating smooth muscle tone by modulating intracellular **sphingosine kinase** mediated signaling. The method of the present invention is useful, inter alia, in the treatment and/or prophylaxis of conditions characterized by aberrant, unwanted or otherwise inappropriate smooth muscle tone, in particular aberrant, unwanted or otherwise inappropriate vascular, bronchial or intestinal smooth muscle tone. In work leading up to the present invention, it has been surprisingly determined that resting tone and myogenic responses in resistance arteries are modulated by altering the expression and activity of **sphingosine kinase**. In particular, **sphingosine kinase** has been identified as the major determinant of microvascular tone and a leading candidate to orchestrate the two main components of the myogenic response. Here, the authors tested whether **sphingosine kinase** (Sphk1) that generates the endogenous sphingolipid mediator sphingosine-1-phosphate (S1P) is part of a signaling cascade to activate the RhoA/Rho kinase pathway. Using a new transfection model, the authors report that resting tone and myogenic responses of isolated resistance arteries increased with forced expression of Sphk1 in smooth muscle cells of these arteries. Overexpression of a dominant neg. Sphk1 mutant or coexpression of dominant neg. mutants of RhoA or Rho kinase together with Sphk1 completely inhibited development of tone and myogenic responses. The tone-increasing effects of a Sphk1 overexpression thus suggest that Sphk1 may play an important role in the control of peripheral resistance. The elucidation of this cellular signaling mechanism now facilitates the rational design of methodol. directed to modulating smooth muscle constriction, in particular vascular, bronchial and intestinal smooth muscle constriction, by regulating the functioning of **sphingosine kinase**.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 8 OF 33 MEDLINE on STN DUPLICATE 6

ACCESSION NUMBER: 2004342307 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15246004
TITLE: An assay for **sphingosine kinase** activity using biotinylated sphingosine and streptavidin-coated membranes.
AUTHOR: Roberts Jane L; Moretti Paul A B; Darrow Andrew L; Derian Claudia K; **Vadas Mathew A; Pitson Stuart M**
CORPORATE SOURCE: Hanson Institute, Division of Human Immunology, Institute of Medical and Veterinary Science, Frome Road, Adelaide, SA 5000, Australia.
SOURCE: Analytical biochemistry, (2004 Aug 1) 331 (1) 122-9. Journal code: 0370535. ISSN: 0003-2697.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 20040713
Last Updated on STN: 20050129
Entered Medline: 20050128

AB **Sphingosine kinase** catalyses the phosphorylation of sphingosine to generate sphingosine 1-phosphate, a lipid signaling molecule implicated in roles in a diverse range of mammalian cell processes through its action as both a ligand for G-protein-coupled cell-surface receptors and an apparent intracellular second messenger. This paper describes a rapid, sensitive, and reproducible assay for **sphingosine kinase** activity using biotinylated sphingosine (biotinyl-Sph) as a substrate and capturing the phosphorylated product with streptavidin-coated membranes. We have shown that both human **sphingosine kinase** 1 and 2 (hSK1 and hSK2) can efficiently phosphorylate biotinyl-Sph, with K(m) values similar to those of sphingosine. The assay utilizing this substrate has high sensitivity for hSK1 and hSK2, with detection limits in the low-femtomole range for both purified recombinant enzymes. Importantly, we have also demonstrated the capacity of this assay to measure endogenous **sphingosine kinase** activity in crude cell extracts and to follow changes in this activity following **sphingosine kinase** activation. Together, these results demonstrate the potential utility of this assay in both cell-based analysis of **sphingosine kinase** signaling pathways and high-throughput screens for agents affecting **sphingosine kinase** activity in vitro.

L20 ANSWER 9 OF 33 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:291898 BIOSIS
DOCUMENT NUMBER: PREV200400291380
TITLE: **Sphingosine kinase** (Sphk1) modulates tone and myogenic responses (MR) in isolated resistance arteries (RA) via activation of RhoA/Rho kinase.
AUTHOR(S): Bolz, Steffen-Sebastian [Reprint Author]; **Pitson, Stuart**; Spiegel, Sarah; Pohl, Ulrich
CORPORATE SOURCE: Institute of Physiology, Ludwig-Maximilians-University, Schillerstrasse 44, Munich, 80336, Germany
bolz@lmu.de
SOURCE: FASEB Journal, (2004) Vol. 18, No. 4-5, pp. Abst. 211.12. http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. Washington, District of Columbia, USA. April 17-21, 2004. FASEB.
ISSN: 0892-6638 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Jun 2004
Last Updated on STN: 23 Jun 2004

AB Sphingosine-1-phosphate (S1P) is a RhoA/Rho kinase-dependent vasoconstrictor of RA. We examined whether the S1P-generating Sphk1 is part of a pressure-induced signalling pathway that activates RhoA/Rho kinase.RA (dia 206+/-9mum) were transfected for 19-22h with plasmids coding for Sphk1, its dominant negative (dn) mutant, hSK^{G82D}, or dominant active RhoA (L63RhoA). Dn RhoA (N19RhoA) or dn Rho kinase (KD1A) were coexpressed with Sphk1 to assess the involvement of the RhoA/Rho kinase pathway in mediating Sphk1 effects. GFP-transfected RA served as control.Resting tone and MRs of RA increased with expression of Sphk1 or L63RhoA in smooth muscle cells. Expression of hSK^{G82D} or coexpression of N19RhoA or KD1A together with Sphk1 inhibited the development of tone and MRs in RA. MRs in L63RhoA-transfected RAs, although stronger than in GFP-transfected, were weaker than in Sphk1-overexpressing RA. Concomitantly, MR-associated increases in (Ca²⁺)_i were unaffected in L63RhoA-transfected,

augmented in Sphk1-overexpressing and delayed in hSK^{G82D}-transfected RAs. Our results show that the Sphk1 modulates RA resting tone via activation of RhoA/Rho kinase. The dual effect of Sphk1 on RhoA/Rho kinase signalling and (Ca²⁺)_i following increases in pressure suggests that the Sphk1 orchestrates these two components of the MR, thus enabling their precise spatio-temporal interaction during this intrinsic process. .

L20 ANSWER 10 OF 33 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:28863 BIOSIS
DOCUMENT NUMBER: PREV200400030039
TITLE: Screening method for an agent having an effect on a **sphingosine kinase** signaling pathway.
AUTHOR(S): Gamble, Jennifer [Inventor, Reprint Author]; **Vadas, Mathew** [Inventor]; Xia, Pu [Inventor]; Barter, Phillip [Inventor]; Rye, Kerry-Anne [Inventor]; **Wattenberg, Brian** [Inventor]; **Pitson, Stuart** [Inventor]
CORPORATE SOURCE: South Australia, Australia
ASSIGNEE: Medvet Science Pty. Ltd., Adelaide, Australia
PATENT INFORMATION: US 6649362 20031118
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov 18 2003) Vol. 1276, No. 3. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Dec 2003
Last Updated on STN: 31 Dec 2003

AB A screening method for identifying a therapeutic candidate for a coronary heart disease or an inflammatory condition is disclosed. The screening method tests for the presence or absence of an effect by a putative therapeutic agent on a component of a **sphingosine kinase** signaling pathway.

L20 ANSWER 11 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:796515 HCAPLUS
DOCUMENT NUMBER: 139:303797
TITLE: Variants of mammalian **sphingosine kinase** with reduced catalytic activity and their use in controlling sphingosine-1-phosphate activated processes
INVENTOR(S): **Pitson, Stuart M.**; Xia, Pu; Moretti, Paul A.; Verwey, Julia R.; **Vadas, Mathew A.**; **Wattenberg, Brian W.**
PATENT ASSIGNEE(S): Medvet Science Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082322	A1	20031009	WO 2003-AU388	20030328

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2480661 AA 20031009 CA 2003-2480661 20030328

EP 1499343 A1 20050126 EP 2003-745226 20030328

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: AU 2002-1448 A 20020328
AU 2002-1538 A 20020405
AU 2002-1621 A 20020408
AU 2002-951668 A 20020919
AU 2003-900230 A 20030121
WO 2003-AU388 W 20030328

AB The present invention relates generally to a method of modulating cellular activity by modulating the activity of **sphingosine kinase** by modulating phosphorylation of the enzyme. Modulating phosphorylation of the enzyme modulates the activity of the enzyme and its ability to catalyze formation of the signaling mol. sphingosine-1-phosphate. The present invention still further extends to **sphingosine kinase** variants and to functional derivs., homologues or analogs, chemical equivalent and mimetics thereof exhibiting reduced and/or ablated capacity to undergo phosphorylation. The method and mols. of the present invention are useful, inter alia, in the treatment and/or prophylaxis of conditions characterized by aberrant, unwanted or otherwise inappropriate cellular and/or **sphingosine kinase** functional activity. The present invention is further directed to methods for identifying and/or designing agents capable of modulating **sphingosine kinase** phosphorylation.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 12 OF 33 MEDLINE on STN DUPLICATE 7

ACCESSION NUMBER: 2003090347 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12480944

TITLE: Sphingosine 1-phosphate and platelet-derived growth factor (PDGF) act via PDGF beta receptor-sphingosine 1-phosphate receptor complexes in airway smooth muscle cells.

AUTHOR: Waters Catherine; Sambi Balwinder; Kong Kok-Choi; Thompson Dawn; **Pitson Stuart M**; Pyne Susan; Pyne Nigel J

CORPORATE SOURCE: Department of Physiology and Pharmacology, Strathclyde Institute for Biomedical Sciences, University of Strathclyde, 27 Taylor St., Glasgow, G4 0NR, Scotland, United Kingdom.

SOURCE: Journal of biological chemistry, (2003 Feb 21) 278 (8) 6282-90. Electronic Publication: 2002-12-11.
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200304

ENTRY DATE: Entered STN: 20030227
Last Updated on STN: 20030423
Entered Medline: 20030422

AB Platelet-derived growth factor (PDGF) and sphingosine 1-phosphate (S1P) act via PDGF beta receptor-S1P(1) receptor complexes in airway smooth muscle cells to promote mitogenic signaling. Several lines of evidence support this conclusion. First, both receptors were co-immunoprecipitated from cell lysates with specific anti-S1P(1) antibodies, indicating that they form a complex. Second, treatment of airway smooth muscle cells with PDGF stimulated the phosphorylation of p42/p44 MAPK, and this phosphorylated p42/p44 MAPK associates with the PDGF beta receptor-S1P(1) receptor complex. Third, treatment of cells with antisense S1P(1)

receptor plasmid construct reduced the PDGF- and S1P-dependent activation of p42/p44 MAPK. Fourth, S1P and/or PDGF induced the formation of endocytic vesicles containing both PDGF beta receptors and S1P(1) receptors, which was required for activation of the p42/p44 MAPK pathway. PDGF does not induce the release of S1P, suggesting the absence of a sequential mechanism. However, **sphingosine kinase** 1 is constitutively exported from cells and supports activation of p42/p44 MAPK by exogenous sphingosine. Thus, the presentation of sphingosine from other cell types and its conversion to S1P by the kinase exported from airway smooth muscle cells might enable S1P to act with PDGF on the PDGF beta receptor-S1P(1) receptor complex to induce biological responses in vivo. These data provide further evidence for a novel mechanism for G-protein-coupled receptor and receptor tyrosine kinase signal integration that is distinct from the transactivation of receptor tyrosine kinases by G-protein-coupled receptor agonists and/or sequential release and action of S1P in response to PDGF.

L20 ANSWER 13 OF 33 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:51191 SCISEARCH
THE GENUINE ARTICLE: 756LU
TITLE: **Sphingosine kinase** transduces estrogen signaling in MCF-7 cells.
AUTHOR: Sukocheva O A (Reprint); Wang L; Albanese N; **Vadas M A**; Xia P
CORPORATE SOURCE: Hanson Inst Canc Res, Adelaide, SA, Australia
COUNTRY OF AUTHOR: Australia
SOURCE: CLINICAL CANCER RESEARCH, (1 DEC 2003) Vol. 9, No. 16, Part 2, Supp. [S], pp. 6238S-6238S.
Publisher: AMER ASSOC CANCER RESEARCH, 615 CHESTNUT ST, 17TH FLOOR, PHILADELPHIA, PA 19106-4404 USA.
ISSN: 1078-0432.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L20 ANSWER 14 OF 33 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 2003510413 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14532121
TITLE: Activation of **sphingosine kinase** 1 by ERK1/2-mediated phosphorylation.
AUTHOR: **Pitson Stuart M**; Moretti Paul A B; Zebol Julia R; Lynn Helen E; Xia Pu; **Vadas Mathew A**; **Wattenberg Binks W**
CORPORATE SOURCE: Hanson Institute, Division of Human Immunology, Institute of Medical and Veterinary Science, Frome Road, Adelaide, SA 5000, Australia.. stuart.pitson@imvs.sa.gov.au
SOURCE: EMBO journal, (2003 Oct 15) 22 (20) 5491-500.
Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20031101
Last Updated on STN: 20040110
Entered Medline: 20040109

AB **Sphingosine kinase** 1 is an agonist-activated signalling enzyme that catalyses the formation of sphingosine 1-phosphate, a lipid second messenger that has been implicated in a number of agonist-driven cellular responses, including stimulation of cell proliferation, inhibition of apoptosis and expression of inflammatory molecules. Although agonist-induced stimulation of **sphingosine**

kinase activity is critical in a number of signalling pathways, nothing has been known of the molecular mechanism of this activation. Here we show that this activation results directly from phosphorylation of **sphingosine kinase** 1 at Ser225, and present several lines of evidence to show compellingly that the activating kinase is ERK1/2 or a close relative. Furthermore, we show that phosphorylation of **sphingosine kinase** 1 at Ser225 results not only in an increase in enzyme activity, but is also necessary for translocation of the enzyme from the cytosol to the plasma membrane. Thus, these studies have elucidated the mechanism of agonist-mediated **sphingosine kinase** activation, and represent a key finding in understanding the regulation of **sphingosine kinase**/sphingosine 1-phosphate-controlled signalling pathways.

L20 ANSWER 15 OF 33 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2003458641 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12881510
TITLE: **Sphingosine kinase** transmits estrogen signaling in human breast cancer cells.
AUTHOR: Sukocheva Olga A; Wang Lijun; Albanese Nathaniel; **Pitson Stuart M; Vadas Mathew A**; Xia Pu
CORPORATE SOURCE: Signal Transduction Laboratory, Division of Human Immunology, Hanson Institute, Institute of Medical and Veterinary Science and University of Adelaide, Adelaide, South Australia 5000, Australia.
SOURCE: Molecular endocrinology (Baltimore, Md.), (2003 Oct) 17 (10) 2002-12. Electronic Publication: 2003-07-24. Journal code: 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20031002
Last Updated on STN: 20040624
Entered Medline: 20040622

AB Current understanding of cytoplasmic signaling pathways that mediate estrogen action in human breast cancer is incomplete. Here we report that treatment with 17beta-estradiol (E2) activates a novel signaling pathway via activation of **sphingosine kinase** (SphK) in MCF-7 breast cancer cells. We found that E2 has dual actions to stimulate SphK activity, i.e. a rapid and transient activation mediated by putative membrane G protein-coupled estrogen receptors (ER) and a delayed but prolonged activation relying on the transcriptional activity of ER. The E2-induced SphK activity consequently activates downstream signal cascades including intracellular Ca2+ mobilization and Erk1/2 activation. Enforced expression of human SphK type 1 gene in MCF-7 cells resulted in increases in SphK activity and cell growth. Moreover, the E2-dependent mitogenesis were highly promoted by SphK overexpression as determined by colony growth in soft agar and solid focus formation. In contrast, expression of SphKG82D, a dominant-negative mutant SphK, profoundly inhibited the E2-mediated Ca2+ mobilization, Erk1/2 activity and neoplastic cell growth. Thus, our data suggest that SphK activation is an important cytoplasmic signaling to transduce estrogen-dependent mitogenic and carcinogenic action in human breast cancer cells.

L20 ANSWER 16 OF 33 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2003343981 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12847068
TITLE: **Sphingosine kinase** modulates microvascular tone and myogenic responses through activation of RhoA/Rho kinase.
AUTHOR: Bolz Steffen-Sebastian; Vogel Lukas; Sollinger Daniel;

Derwand Roland; Boer Christa; **Pitson Stuart M**; Spiegel Sarah; Pohl Ulrich

CORPORATE SOURCE: Institute of Physiology, Ludwig Maximilians University, Schillerstrasse 44, 80336 Muenchen, Germany.. bolz@lrz.uni-muenchen.de

SOURCE: Circulation, (2003 Jul 22) 108 (3) 342-7. Electronic Publication: 2003-07-07. Journal code: 0147763. ISSN: 1524-4539.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200308

ENTRY DATE: Entered STN: 20030724
Last Updated on STN: 20030814
Entered Medline: 20030813

AB BACKGROUND: RhoA and Rho kinase are important modulators of microvascular tone. METHODS AND RESULTS: We tested whether **sphingosine kinase** (Sphk1) that generates the endogenous sphingolipid mediator sphingosine-1-phosphate (S1P) is part of a signaling cascade to activate the RhoA/Rho kinase pathway. Using a new transfection model, we report that resting tone and myogenic responses of isolated resistance arteries increased with forced expression of Sphk1 in smooth muscle cells of these arteries. Overexpression of a dominant negative Sphk1 mutant or coexpression of dominant negative mutants of RhoA or Rho kinase together with Sphk1 completely inhibited development of tone and myogenic responses. CONCLUSIONS: The tone-increasing effects of a Sphk1 overexpression suggest that Sphk1 may play an important role in the control of peripheral resistance.

L20 ANSWER 17 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:946141 HCAPLUS

DOCUMENT NUMBER: 138:38089

TITLE: **Sphingosine kinase** interacts with TRAF2 and modulates tumor necrosis factor-induced cellular activity

INVENTOR(S): Xia, Pu; Wang, Lijun; **Vadas, Mathew**; Gamble, Jennifer; Moretti, Paul; **Pitson, Stuart**

PATENT ASSIGNEE(S): Medvet Science Pty. Ltd., Australia

SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098458	A1	20021212	WO 2002-AU710	20020603
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2449487	AA	20021212	CA 2002-2449487	20020603
EP 1404364	A1	20040407	EP 2002-732213	20020603
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

JP 2005502598	T2	20050127	JP 2003-501495		20020603
US 2005100547	A1	20050512	US 2003-479933		20020603
PRIORITY APPLN. INFO.:			AU 2001-5521	A	20010607
			AU 2001-6978	A	20010813
			AU 2001-9759	A	20011227
			WO 2002-AU710	W	20020603

AB The present invention relates generally to a method of modulating cytokine-mediated cellular activity and to agents useful for same. The invention is based on the discovery of interaction between the C-terminal PPEE sequence of **sphingosine kinase** and tumor necrosis factor receptor-associated factor 2 (TRAF2). More particularly, the present invention contemplates a method of modulating tumor necrosis factor-mediated cellular activity by modulating an intracellular **sphingosine kinase**-dependent signalling mechanism. The method of the present invention is useful, inter alia, in the treatment and/or prophylaxis of conditions characterized by aberrant, unwanted or otherwise inappropriate cytokine-mediated cellular activity The present invention is further directed to methods for identifying and/or designing agents capable of modulating the subject **sphingosine kinase**-dependent signalling mechanism.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 18 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:10690 HCAPLUS

DOCUMENT NUMBER: 136:81963

TITLE: Molecular variants of mammalian **sphingosine kinase** with reduced catalytic activity and therapeutic uses thereof

INVENTOR(S): **Pitson, Stuart**; Moretti, Paul; Zebol, Julia; Xia, Pu; Gamble, Jennifer; **Vadas, Mathew**; D'Andrea, Richard; **Wattenberg, Binks**

PATENT ASSIGNEE(S): Medvet Science Pty. Ltd., Australia

SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000887	A1	20020103	WO 2001-AU730	20010620
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2414210	AA	20020103	CA 2001-2414210	20010620
AU 2001065699	A5	20020108	AU 2001-65699	20010620
EP 1299548	A1	20030409	EP 2001-942904	20010620
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004500903	T2	20040115	JP 2002-506202	20010620
BR 2001012059	A	20040727	BR 2001-12059	20010620
NZ 523343	A	20050324	NZ 2001-523343	20010620
NO 2002006265	A	20030224	NO 2002-6265	20021227
ZA 2003000214	A	20040408	ZA 2003-214	20030108
PRIORITY APPLN. INFO.:			AU 2000-8408	A 20000628

AU 2000-8699	A	20000711
AU 2000-9980	A	20000908
AU 2001-2749	A	20010129
WO 2001-AU730	W	20010620

AB The present invention relates generally to a **sphingosine kinase** variant and to derivs., analogs, chemical equivalent and mimetics thereof exhibiting reduced catalytic activity and, more particularly, to **sphingosine kinase** variants which exhibit a reduced capacity to phosphorylate sphingosine to sphingosine-1-phosphate. The present invention also contemplates genetic sequences encoding said **sphingosine kinase** variants and derivs., analogs and mimetics thereof. The variants of the present invention are useful in a range of therapeutic and prophylactic applications. Site-directed mutagenesis of a putative ATP-binding site (glycine in position 82 to aspartic acid, G82D) resulted in a catalytically inactive **sphingosine kinase** (SK) for phosphorylating sphingosine to sphingosine-1-phosphate. The G82D SK is expressed, as shown by Western blots, and does not suppress endogenous cellular SK activity. However, G82D SK decreases activation of **sphingosine kinase** activity after treatment of cells with agents such as TNF, IL-1, and PMA and it inhibits SK activity that is stimulated by the Ras oncogene. Another mutant G82A (glycine at position 82 substituted with alanine) retains about 5% of the wild-type level of catalytic activity. Anal. of substrate kinetics of G82A SK shows low affinity for ATP but wild-type affinity for sphingosine.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 19 OF 33 MEDLINE on STN DUPLICATE 11

ACCESSION NUMBER: 2002731982 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12393916
TITLE: The nucleotide-binding site of human **sphingosine kinase** 1.
AUTHOR: **Pitson Stuart M**; Moretti Paul A B; Zebol Julia R; Zareie Reza; Derian Claudia K; Darrow Andrew L; Qi Jenson; D'Andrea Richard J; Bagley Christopher J; **Vadas Mathew A**; **Wattenberg Binks W**
CORPORATE SOURCE: Hanson Institute, Division of Human Immunology, Institute of Medical and Veterinary Science, Frome Road, Adelaide SA 5000, Australia.. stuart.pitson@imvs.sa.gov.asu
SOURCE: Journal of biological chemistry, (2002 Dec 20) 277 (51) 49545-53. Electronic Publication: 2002-10-18. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20021227
Last Updated on STN: 20030214
Entered Medline: 20030212

AB **Sphingosine kinase** catalyzes the formation of sphingosine 1-phosphate, a lipid second messenger that has been implicated in a number of agonist-driven cellular responses including mitogenesis, anti-apoptosis, and expression of inflammatory molecules. Despite the importance of **sphingosine kinase**, very little is known regarding its structure or mechanism of catalysis. Moreover, **sphingosine kinase** does not contain recognizable catalytic or substrate-binding sites, based on sequence motifs found in other kinases. Here we have elucidated the nucleotide-binding site of human **sphingosine kinase** 1 (hSK1) through a combination of site-directed mutagenesis and affinity labeling with the ATP analogue, FSBA. We have shown that Gly(82) of hSK1 is involved in ATP

binding since mutation of this residue to alanine resulted in an enzyme with an approximately 45-fold higher K(m)((ATP)). We have also shown that Lys(103) is important in catalysis since an alanine substitution of this residue ablates catalytic activity. Furthermore, we have shown that this residue is covalently modified by FSBA. Our data, combined with amino acid sequence comparison, suggest a motif of SGDGX(17-21)K is involved in nucleotide binding in the **sphingosine kinases**. This motif differs in primary sequence from all previously identified nucleotide-binding sites. It does, however, share some sequence and likely structural similarity with the highly conserved glycine-rich loop, which is known to be involved in anchoring and positioning the nucleotide in the catalytic site of many protein kinases.

L20 ANSWER 20 OF 33 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2002139136 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11777919
TITLE: **Sphingosine kinase** interacts with TRAF2 and dissects tumor necrosis factor-alpha signaling.
AUTHOR: Xia Pu; Wang Lijun; Moretti Paul A B; Albanese Nathaniel; Chai Fugui; **Pitson Stuart M**; D'Andrea Richard J; Gamble Jennifer R; **Vadas Mathew A**
CORPORATE SOURCE: Division of Human Immunology, The Hanson Institute, Institute of Medical and Veterinary Science and University of Adelaide, Frome Road, Adelaide SA 5000, Australia.. pu.xia@imvs.sa.gov
SOURCE: Journal of biological chemistry, (2002 Mar 8) 277 (10) 7996-8003. Electronic Publication: 2002-01-02. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020305
Last Updated on STN: 20030105
Entered Medline: 20020415

AB Tumor necrosis factor-alpha (TNF) receptor-associated factor 2 (TRAF2) is one of the major mediators of TNF receptor superfamily transducing TNF signaling to various functional targets, including activation of NF-kappa B, JNK, and antiapoptosis. We investigated how TRAF2 mediates differentially the distinct downstream signals. We now report a novel mechanism of TRAF2-mediated signal transduction revealed by an association of TRAF2 with **sphingosine kinase** (SphK), a lipid kinase that is responsible for the production of sphingosine 1-phosphate. We identified a TRAF2-binding motif of SphK that mediated the interaction between TRAF2 and SphK resulting in the activation of the enzyme, which in turn is required for TRAF2-mediated activation of NF-kappa B but not JNK. In addition, by using a kinase inactive dominant-negative SphK and a mutant SphK that lacks TRAF2-binding motif we show that the interaction of TRAF2 with SphK and subsequent activation of SphK are critical for prevention of apoptosis during TNF stimulation. These findings show a role for SphK in the signal transduction by TRAF2 specifically leading to activation of NF-kappa B and antiapoptosis.

L20 ANSWER 21 OF 33 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:431791 BIOSIS
DOCUMENT NUMBER: PREV200200431791
TITLE: Transfection of **sphingosine kinase** in resistance arteries (RA) increases myogenic tone via activation of the RhoA/Rho kinase pathway.
AUTHOR(S): Bolz, Steffen-Sebastian [Reprint author]; Vogel, Lukas [Reprint author]; Sollinger, Daniel [Reprint author];

Derwand, Roland [Reprint author]; **Pitson, Stuart**; Pohl, Ulrich [Reprint author]

CORPORATE SOURCE: Institute of Physiology, Ludwig Maximilians University, Schillerstrasse 44, Munich, 80366, Germany

SOURCE: FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1119. print.
Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002.
CODEN: FAJOEC. ISSN: 0892-6638.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 14 Aug 2002
Last Updated on STN: 14 Aug 2002

AB The Rho/Rho kinase pathway is an important modulator of microvascular tone. We tested whether endogenous sphingosine-1-phosphate (S1P) stimulates this pathway and whether it affects resting tone (rT) and myogenic responses (MR). RA were incubated for 19-22h with plasmids coding for the S1P-generating enzyme **sphingosine kinase** (Sphk) or an inactive mutant (hSK-G82D). Dominant active (L63RhoA) or inactive (N19RhoA) RhoA and Rho kinase (KD1A) mutants were coexpressed with Sphk to assess their involvement in mediating Sphk effects. GFP (green fluorescent protein)-transfected RA served as controls. rT was enhanced in RA expressing Sphk (-23+-3% of maximum diameter vs. -10+-11% in RAGFP, $p<0.01$) and L63RhoA (-22+-2%) but almost abolished in hSK-G82D-transfected RA (-2%). Coexpression of N19RhoA or KD1A abolished development of rT. MR (pressure step from 45 to 110mmHg) were enhanced by Sphk and L63RhoA (-154+-14% and -92+-12% of initial distension vs. -61+-8% in RAGFP, $p<0.01$) but almost completely inhibited after coexpression of N19RhoA or KD1A or transfection with hSK-G82D. The ability of endogenous Sphk to activate the Rho/Rho kinase pathway implicates a possible important role for the development of hypertension.

L20 ANSWER 22 OF 33 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:80622 BIOSIS

DOCUMENT NUMBER: PREV200300080622

TITLE: Transfection of **sphingosine kinase** into vascular smooth muscle cells of isolated resistance arteries increases myogenic tone via activation of the RhoA/Rho kinase pathway.

AUTHOR(S): Bolz, Steffen-Sebastian [Reprint Author]; Vogel, Lukas [Reprint Author]; Sollinger, Daniel [Reprint Author]; Derwand, Roland [Reprint Author]; Boer, Christa; **Pitson, Stuart**; Spiegel, Sarah; Pohl, Ulrich [Reprint Author]

CORPORATE SOURCE: Ludwig Maximilians Univ, Munich, Germany

SOURCE: Circulation, (November 5 2002) Vol. 106, No. 19 Supplement, pp. II-271. print.
Meeting Info.: Abstracts from Scientific Sessions. Chicago, IL, USA. November 17-20, 2002. American Heart Association.
ISSN: 0009-7322 (ISSN print).

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 6 Feb 2003
Last Updated on STN: 4 Mar 2003

L20 ANSWER 23 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:833523 HCAPLUS

DOCUMENT NUMBER: 135:356367

TITLE: Role of **sphingosine kinase** in

oncogenesis, and use in cancer therapy

INVENTOR(S): **Vadas, Mathew**; Gamble, Jennifer; Xia, Pu; Wang, Lijun

PATENT ASSIGNEE(S): Medvet Science Pty. Ltd., Australia

SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085953	A1	20011115	WO 2001-AU539	20010511
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2408196	AA	20011115	CA 2001-2408196	20010511
EP 1290182	A1	20030312	EP 2001-929118	20010511
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001010759	A	20030506	BR 2001-10759	20010511
JP 2003532423	T2	20031105	JP 2001-582542	20010511
ZA 2002009066	A	20040407	ZA 2002-9066	20021107
NO 2002005375	A	20030107	NO 2002-5375	20021108
US 2004014635	A1	20040122	US 2003-275686	20030625

PRIORITY APPLN. INFO.: AU 2000-7447 A 20000511
WO 2001-AU539 W 20010511

AB The present invention relates generally to a method of modulating the growth of cells and, more particularly, to a method of down-regulating the growth of neoplastic cells. The present invention is useful, inter alia, in the therapeutic and/or prophylactic treatment of cancers such as, but not limited to, solid cancers such as cancers of the colon, stomach, lung, brain, bone, esophagus, pancreas, breast, ovary or uterus. **Sphingosine kinase** (SphK) is a highly conserved lipid kinase that phosphorylates sphingosine to form sphingosine-1-phosphate (S1P). S1P/SphK has been implicated as a signaling pathway to regulate diverse cellular functions, including cell growth, proliferation and survival. The authors report that cells overexpressing SphK have increased enzymic activity and acquire the transformed phenotype, as determined by focus formation, colony growth in soft agar and the ability to form tumors in NOD/SCID mice. Using a chemical inhibitor of SphK, or an SphK mutant that inhibits enzyme activation, the authors found that SphK activity is involved in oncogenic H-Ras-mediated transformation, suggesting a novel signaling pathway for Ras activation. This is the first demonstration that a wild-type lipid kinase gene acts as an oncogene. The findings not only point to a new signaling pathway in transformation but also to the potential of SphK inhibitors in cancer therapy.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 24 OF 33 EMBASE
on STN

ACCESSION NUMBER: 2001273878 EMBASE

TITLE: Novel mechanisms of the transendothelial migration of

leukocytes.
AUTHOR: Imhof B.A.; Engelhardt B.; **Vadas M.A.**
CORPORATE SOURCE: B.A. Imhof, Dept. of Pathology, Centre Medical Universitaire, 1 Rue Michel-Servet, 1211 Geneva 4, Switzerland. Beat.Imhof@medecine.unige.ch
SOURCE: Trends in Immunology, (1 Aug 2001) Vol. 22, No. 8, pp. 411-414.
Refs: 8
ISSN: 1471-4906 CODEN: TIRMAE
PUBLISHER IDENT.: S 1471-4906(01)01961-5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 20010823
Last Updated on STN: 20010823

L20 ANSWER 25 OF 33 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 2001700595 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11741582
TITLE: A point mutant of human **sphingosine kinase** 1 with increased catalytic activity.
AUTHOR: **Pitson S M**; Moretti P A; Zebol J R; **Vadas M A**; D'Andrea R J; **Wattenberg B W**
CORPORATE SOURCE: Hanson Centre for Cancer Research, Division of Human Immunology, Institute of Medical and Veterinary Science, Frome Road, Adelaide, SA 5000, Australia..
stuart.pitson@imvs.sa.gov.au
SOURCE: FEBS letters, (2001 Dec 7) 509 (2) 169-73.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011220
Last Updated on STN: 20020125
Entered Medline: 20020117

AB **Sphingosine kinase** (SK) catalyses the formation of sphingosine 1-phosphate, a lipid second messenger that has been implicated in mediating such fundamental biological processes as cell growth and survival. Very little is currently known regarding the structure or mechanisms of catalysis and activation of SK. Here we have tested the functional importance of Gly(113), a highly conserved residue of human **sphingosine kinase** 1 (hSK), by site-directed mutagenesis. Surprisingly, a Gly(113)-->Ala substitution generated a mutant that had 1.7-fold greater catalytic activity than wild-type hSK (hSK(WT)). Our data suggests that the Gly(113)-->Ala mutation increases catalytic efficiency of hSK, probably by inducing a conformational change that increases the efficiency of phosphoryl transfer. Interestingly, hSK(G113A) activity could be stimulated in HEK293T cells by cell agonists to a comparable extent to hSK(WT).

L20 ANSWER 26 OF 33 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
DUPLICATE 14
ACCESSION NUMBER: 2001-03254 BIOTECHDS
TITLE: Novel **sphingosine-kinase** protein and nucleic acid molecules for diagnosis, prophylaxis and treatment of rheumatoid arthritis, asthma, atherosclerosis, inflammation, meningitis, multiple sclerosis and septic shock ;

involving vector plasmid pGEM4Z-mediated gene transfer for

expression in Escherichia coli

AUTHOR: **Pitson S M**; **Wattenberg B W**; D'Andrea R J; **Gamble J R**; **Vadas M A**
PATENT ASSIGNEE: Johnson+Johnson
LOCATION: Everleigh, New South Wales, Australia.
PATENT INFO: WO 2000070028 23 Nov 2000
APPLICATION INFO: WO 2000-AU457 12 May 2000
PRIORITY INFO: AU 1999-1504 8 Jul 1999; AU 1999-339 13 May 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-016227 [02]

AB An isolated **sphingosine-kinase** protein (I) or its derivative, analog, chemical equivalent or mimetic, is new. Also claimed are: an isolated nucleic acid molecule (II) or its derivative or analog comprising a nucleotide sequence encoding or complementary to a sequence encoding (I); an agent for use in modulating **sphingosine-kinase** activity or expression; a pharmaceutical composition (I) or the agent; an isolated antibody directed to (I) or (II); and diagnosing or monitoring a mammalian disease condition by screening for (I) in a biological sample isolated from the mammal. (I), (II) and the agent are useful for modulating expression, functional activity or cellular functional activity of **sphingosine-kinase** in a subject and also treating a mammal by modulating the activity of **sphingosine-kinase**. Diseases treated by regulating **sphingosine-kinase** cellular activity include rheumatoid arthritis, asthma, atherosclerosis, inflammation, meningitis, multiple sclerosis and septic shock. Recombinant human **sphingosine-kinase** was expressed by transforming the vector plasmid pGEM4Z into Escherichia coli BL21. (100pp)

L20 ANSWER 27 OF 33 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 2001038285 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10944534
TITLE: Expression of a catalytically inactive **sphingosine kinase** mutant blocks agonist-induced **sphingosine kinase** activation. A dominant-negative **sphingosine kinase**.
AUTHOR: **Pitson S M**; Moretti P A; Zebol J R; Xia P; **Gamble J R**; **Vadas M A**; D'Andrea R J; **Wattenberg B W**
CORPORATE SOURCE: Hanson Centre for Cancer Research, Division of Human Immunology, Institute of Medical and Veterinary Science and the Department of Medicine, University of Adelaide, Frome Road, Adelaide, SA 5000, Australia.
SOURCE: Journal of biological chemistry, (2000 Oct 27) 275 (43) 33945-50.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001124

AB **Sphingosine kinase** (SK) catalyzes the formation of sphingosine 1-phosphate (S1P), a lipid messenger that plays an important role in a variety of mammalian cell processes, including inhibition of apoptosis and stimulation of cell proliferation. Basal levels of S1P in cells are generally low but can increase rapidly when cells are exposed to various agonists through rapid and transient activation of SK activity. To date, elucidation of the exact signaling pathways affected by these elevated S1P levels has relied on the use of SK inhibitors that are known

to have direct effects on other enzymes in the cell. Furthermore, these inhibitors block basal SK activity, which is thought to have a housekeeping function in the cell. To produce a specific inhibitor of SK activation we sought to generate a catalytically inactive, dominant-negative SK. This was accomplished by site-directed mutagenesis of Gly(82) to Asp of the human SK, a residue identified through sequence similarity to the putative catalytic domain of diacylglycerol kinase. This mutant had no detectable SK activity when expressed at high levels in HEK293T cells. Activation of endogenous SK activity by tumor necrosis factor-alpha (TNFalpha), interleukin-1beta, and phorbol esters in HEK293T cells was blocked by expression of this inactive **sphingosine kinase** (hSK(G82D)). Basal SK activity was unaffected by expression of hSK(G82D). Expression of hSK(G82D) had no effect on TNFalpha-induced activation of protein kinase C and sphingomyelinase activities. Thus, hSK(G82D) acts as a specific dominant-negative SK to block SK activation. This discovery provides a powerful tool for the elucidation of the exact signaling pathways affected by elevated S1P levels following SK activation. To this end we have employed the dominant-negative SK to demonstrate that TNFalpha activation of extracellular signal-regulated kinases 1 and 2 (ERK1,2) is dependent on SK activation.

L20 ANSWER 28 OF 33 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 2001115700 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11114522
TITLE: An oncogenic role of **sphingosine kinase**

AUTHOR: Xia P; **Gamble J R**; Wang L; **Pitson S M**; Moretti P A; **Wattenberg B W**; D'Andrea R J; **Vadas M A**
CORPORATE SOURCE: Division of Human Immunology, Hanson Centre for Cancer Research, Institute of Medical and Veterinary Science and University of Adelaide, Frome Road, SA 5000,., Adelaide, Australia.. pu.xia@imvs.sa.gov.au
SOURCE: Current biology : CB, (2000 Nov 30) 10 (23) 1527-30. Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010215

AB **Sphingosine kinase** (SphK) is a highly conserved lipid kinase that phosphorylates sphingosine to form sphingosine-1-phosphate (S1P). S1P/SphK has been implicated as a signalling pathway to regulate diverse cellular functions [1-3], including cell growth, proliferation and survival [4-8]. We report that cells overexpressing SphK have increased enzymatic activity and acquire the transformed phenotype, as determined by focus formation, colony growth in soft agar and the ability to form tumours in NOD/SCID mice. This is the first demonstration that a wild-type lipid kinase gene acts as an oncogene. Using a chemical inhibitor of SphK, or an SphK mutant that inhibits enzyme activation, we found that SphK activity is involved in oncogenic H-Ras-mediated transformation, suggesting a novel signalling pathway for Ras activation. The findings not only point to a new signalling pathway in transformation but also to the potential of SphK inhibitors in cancer therapy.

L20 ANSWER 29 OF 33 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 2001097784 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10947957
TITLE: Human **sphingosine kinase**: purification,

molecular cloning and characterization of the native and recombinant enzymes.

AUTHOR: **Pitson S M**; D'andrea R J; Vandeleur L; Moretti P A; Xia P; **Gamble J R**; **Vadas M A**; **Wattenberg B W**

CORPORATE SOURCE: Hanson Centre for Cancer Research, Division of Human Immunology, Institute of Medical and Veterinary Science, Frome Road, Adelaide 5000, SA, Australia.

SOURCE: Biochemical journal, (2000 Sep 1) 350 Pt 2 429-41. Journal code: 2984726R. ISSN: 0264-6021.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-AF200328

ENTRY MONTH: 200102

ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201

AB Sphingosine 1-phosphate (S1P) is a novel lipid messenger that has important roles in a wide variety of mammalian cellular processes including growth, differentiation and death. Basal levels of S1P in mammalian cells are generally low, but can increase rapidly and transiently when cells are exposed to mitogenic agents and other stimuli. This increase is largely due to increased activity of **sphingosine kinase** (SK), the enzyme that catalyses its formation. In the current study we have purified, cloned and characterized the first human SK to obtain a better understanding of its biochemical activity and possible activation mechanisms. The enzyme was purified to homogeneity from human placenta using ammonium sulphate precipitation, anion-exchange chromatography, calmodulin-affinity chromatography and gel-filtration chromatography. This resulted in a purification of over 10(6)-fold from the original placenta extract. The enzyme was cloned and expressed in active form in both HEK-293T cells and Escherichia coli, and the recombinant E. coli-derived SK purified to homogeneity. To establish whether post-translational modifications lead to activation of human SK activity we characterized both the purified placental enzyme and the purified recombinant SK produced in E. coli, where such modifications would not occur. The premise for this study was that post-translational modifications are likely to cause conformational changes in the structure of SK, which may result in detectable changes in the physico-chemical or catalytic properties of the enzyme. Thus the enzymes were characterized with respect to substrate specificity and kinetics, inhibition kinetics and various other physico-chemical properties. In all cases, both the native and recombinant SKs displayed remarkably similar properties, indicating that post-translational modifications are not required for basal activity of human SK.

L20 ANSWER 30 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:193987 HCAPLUS

DOCUMENT NUMBER: 130:232524

TITLE: A method of modulating cellular activity

INVENTOR(S): **Vadas, Mathew**; Gamble, Jennifer; Xia, Pu; Barter, Philip; Rye, Kerry-Anne; **Wattenberg, Brian**; **Pitson, Stuart**

PATENT ASSIGNEE(S): Medvet Science Pty. Ltd., Australia

SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9912533	A1	19990318	WO 1998-AU730	19980908
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2302838	AA	19990318	CA 1998-2302838	19980908
AU 9889658	A1	19990329	AU 1998-89658	19980908
AU 757358	B2	20030220		
EP 1011654	A1	20000628	EP 1998-941157	19980908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001515857	T2	20010925	JP 2000-510431	19980908
US 2002051777	A1	20020502	US 2001-977217	20011016
US 6649362	B2	20031118		
US 2005074830	A1	20050407	US 2003-679485	20031007
PRIORITY APPLN. INFO.:			AU 1997-9002	A 19970908
			WO 1998-AU730	W 19980908
			US 2000-508249	A1 20000601
			US 2001-977217	A3 20011016

AB The present invention relates generally to a method of modulating cellular activity and agents useful for same. More particularly, the present invention contemplates a method of modulating endothelial cell activity and even more particularly endothelial cell adhesion mol. expression. Most particularly, the present invention provides a method of treating conditions involving inflammatory mechanisms such as coronary heart disease by preventing or reducing endothelial cell adhesion mol. expression. One aspect of the invention is administration of an agent which modulates one or more components of the **sphingosine kinase** signaling pathway (such as **sphingosine kinase** or sphingosine-1-phosphate). The inhibitory effect of high-d. lipoproteins (HDL) on the **sphingosine kinase** signaling pathway was determined A further aspect of the invention is a method for detecting **sphingosine kinase** activity using 33P-ATP and sphingosine in the presence of a scintillant.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 31 OF 33 MEDLINE on STN DUPLICATE 18

ACCESSION NUMBER: 2000036602 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10567432
TITLE: Activation of **sphingosine kinase** by tumor necrosis factor-alpha inhibits apoptosis in human endothelial cells.
AUTHOR: Xia P; Wang L; **Gamble J R**; **Vadas M A**
CORPORATE SOURCE: Division of Human Immunology, The Hanson Centre for Cancer Research, Adelaide, South Australia 5000, Australia.
SOURCE: Journal of biological chemistry, (1999 Nov 26) 274 (48) 34499-505.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113

Entered Medline: 19991229

AB Human umbilical vein endothelial cells (HUVEC), like most normal cells, are resistant to tumor necrosis factor-alpha (TNF)-induced apoptosis in spite of TNF activating sphingomyelinase and generating ceramide, a known inducer of apoptosis. Here we report that TNF activates another key enzyme, **sphingosine kinase** (SphK), in the sphingomyelin metabolic pathway resulting in production of sphingosine-1-phosphate (S1P) and that S1P is a potent antagonist of TNF-mediated apoptosis. The TNF-induced SphK activation is independent of sphingomyelinase and ceramidase activities, suggesting that TNF affects this enzyme directly other than through a mass effect on sphingomyelin degradation. In contrast to normal HUVEC, in a spontaneously transformed endothelial cell line (C11) TNF stimulation failed to activate SphK and induced apoptosis as characterized by morphological and biochemical criteria. Addition of exogenous S1P or increasing endogenous S1P by phorbol ester markedly protected C11 cell line from TNF-induced apoptosis. Conversely, N, N-dimethylsphingosine, an inhibitor of SphK, profoundly sensitized normal HUVEC to killing by TNF. Thus, we demonstrate that the activation of SphK by TNF is an important signaling for protection from the apoptotic effect of TNF in endothelial cells.

L20 ANSWER 32 OF 33 MEDLINE on STN DUPLICATE 19

ACCESSION NUMBER: 2000020293 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10551885
TITLE: High density lipoproteins (HDL) interrupt the **sphingosine kinase** signaling pathway. A possible mechanism for protection against atherosclerosis by HDL.
AUTHOR: Xia P; **Vadas M A**; Rye K A; Barter P J; **Gamble J R**
CORPORATE SOURCE: Division of Human Immunology, Hanson Centre for Cancer Research, Institute of Medical Science, University of Adelaide, Adelaide, South Australia 5000, Australia.
SOURCE: Journal of biological chemistry, (1999 Nov 12) 274 (46) 33143-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000103

AB The ability of high density lipoproteins (HDL) to inhibit cytokine-induced adhesion molecule expression has been demonstrated in their protective function against the development of atherosclerosis and associated coronary heart disease. A key event in atherogenesis is endothelial activation induced by a variety of stimuli such as tumor necrosis factor-alpha (TNF), resulting in the expression of various adhesion proteins. We have recently reported that sphingosine 1-phosphate, generated by **sphingosine kinase** activation, is a key molecule in mediating TNF-induced adhesion protein expression. We now show that HDL profoundly inhibit TNF-stimulated **sphingosine kinase** activity in endothelial cells resulting in a decrease in sphingosine 1-phosphate production and adhesion protein expression. HDL also reduced TNF-mediated activation of extracellular signal-regulated kinases and NF-kappaB signaling cascades. Furthermore, HDL enhanced the cellular levels of ceramide which in turn inhibits endothelial activation. Thus, the regulation of sphingolipid signaling in endothelial cells by HDL provides a novel insight into the mechanism of protection against atherosclerosis.

L20 ANSWER 33 OF 33 MEDLINE on STN DUPLICATE 20
ACCESSION NUMBER: 1999045661 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9826677
TITLE: Tumor necrosis factor-alpha induces adhesion molecule expression through the **sphingosine kinase** pathway.
AUTHOR: Xia P; **Gamble J R**; Rye K A; Wang L; Hii C S; Cockerill P; Khew-Goodall Y; Bert A G; Barter P J; **Vadas M A**
CORPORATE SOURCE: Division of Human Immunology, The Hanson Centre for Cancer Research, Institute of Medical and Veterinary Science and University of Adelaide, Adelaide, SA 5000, Australia.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1998 Nov 24) 95 (24) 14196-201. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981228

AB The signaling pathways that couple tumor necrosis factor-alpha (TNFalpha) receptors to functional, especially inflammatory, responses have remained elusive. We report here that TNFalpha induces endothelial cell activation, as measured by the expression of adhesion protein E-selectin and vascular adhesion molecule-1, through the **sphingosine kinase** (SKase) signaling pathway. Treatment of human umbilical vein endothelial cells with TNFalpha resulted in a rapid SKase activation and sphingosine 1-phosphate (S1P) generation. S1P, but not ceramide or sphingosine, was a potent dose-dependent stimulator of adhesion protein expression. S1P was able to mimic the effect of TNFalpha on endothelial cells leading to extracellular signal-regulated kinases and NF-kappaB activation, whereas ceramide or sphingosine was not. Furthermore, N, N-dimethylsphingosine, an inhibitor of SKase, profoundly inhibited TNFalpha-induced extracellular signal-regulated kinases and NF-kappaB activation and adhesion protein expression. Thus we demonstrate that the SKase pathway through the generation of S1P is critically involved in mediating TNFalpha-induced endothelial cell activation.

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(FILE 'HOME' ENTERED AT 10:16:41 ON 23 JUN 2005)

FILE 'STNGUIDE' ENTERED AT 10:16:54 ON 23 JUN 2005

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 10:17:40 ON 23 JUN 2005

L1 22912 S SPHINGOSINE
L2 1950 S L1 (W)KINASE?
L3 104 S HUMAN (W)L2
L4 54 DUP REM L3 (50 DUPLICATES REMOVED)
L5 7132348 S CLON? OR EXPRESS? OR RECOMBINANT
L6 36 S L4 AND L5
L7 3507345 S MIMETIC? OR DERIVATIVE? OR ANALOGUE?
L8 388 S L2 AND L7
L9 6947 S SPHINGOSINE-1-PHOSPHATE
L10 320 S L8 AND L9
L11 320 S L10 AND KINASE?
L12 211 DUP REM L11 (109 DUPLICATES REMOVED)
L13 126 S HUMAN AND L12

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                E PITSON S M/AU
L14          170 S E3-E7
                E WATTENBERG B W/AU
L15          174 S E3-E9
                E DIANDREA R J/AU
                E GAMBLE J R/AU
L16          355 S E3
                E VADAS M A/AU
L17         1272 S E3-E8
L18         1564 S L14 OR L15 OR L16 OR L17
L19          109 S L2 AND L18
L20           33 DUP REM L19 (76 DUPLICATES REMOVED)
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	L #	Hits	Search Text
1	L1	1	"6730480".pn.
2	L2	81713	analogue$2
3	L3	1	l1 and l2
4	L4	123	sphingosine adj kinase$2
5	L5	490492	human
6	L6	53	l4 same l5
7	L7	744145	clon$3 or express$3 or recombinant
8	L8	37	l6 same l7
9	L9	57618	analogue? or deri9vative? or mimetic$2
10	L10	406851	analogue? or derivative? or mimetic$2
11	L11	3	l8 same l10
12	L12	23923	PITSON WATTENBERG XIA GAMBLE VADAS
13	L13	30	l4 and l12

	Issue Date	Pages	Document ID	Title
1	20050113	35	US 20050009732 A1	Method of treatment and agents useful for same
2	20041209	54	US 20040247603 A1	Compositions and methods for the treatment and prevention of cancer, angiogenesis, and inflammation
3	20041028	34	US 20040214319 A1	Methods of regulating differentiation in stem cells
4	20041014	42	US 20040203104 A1	Mammalian sphingosine kinase type 2 isoforms, cloning, expression and methods of use thereof
5	20040708	58	US 20040132053 A1	Sphingosine kinase enzyme
6	20040701	101	US 20040126834 A1	Compositions and methods for the modulation of sphingolipid metabolism and/or signaling
7	20040624	31	US 20040120961 A1	Saposin C and receptors as targets for treatment of benign and malignant disorders
8	20040506	26	US 20040086487 A1	Induction of blood vessel formation through administration of polynucleotides encoding sphingosine kinases
9	20040325	82	US 20040058325 A1	Gene expression in biological conditions
10	20040318	287	US 20040053245 A1	Novel nucleic acids and polypeptides
11	20040219	30	US 20040034075 A1	Sphingosine kinase inhibitors
12	20040122	230	US 20040016025 A1	Rice promoters for regulation of plant expression

	Issue Date	Pages	Document ID	Title
13	20040108	345	US 20040005563 A1	Methods of diagnosis of ovarian cancer, compositions and methods of screening for modulators of ovarian cancer
14	20031127	81	US 20030219782 A1	Compositions and methods for the modulation of sphingolipid metabolism and/or signaling
15	20031009	40	US 20030190650 A1	Screening method
16	20030918	49	US 20030175939 A1	Sphingosine-1-phosphate lyase polypeptides, polynucleotides and modulating agents and methods of use therefor
17	20030911	41	US 20030170245 A1	Activation of matriptase and diagnostic and therapeutic methods based thereon
18	20030821	80	US 20030157082 A1	Methods and compositions for treating cancer using 140, 1470, 1686, 2089, 2427, 3702, 5891, 6428, 7181, 7660, 25641, 69583, 49863, 8897, 1682, 17667, 9235, 3703, 14171, 10359, 1660, 1450, 18894, 2088, 32427, 2160, 9252, 9389, 1642, 85269, 10297, 1584, 9525, 14124, 4469, 8990, 2100, 9288, 64698, 10480,20893, 33230,1586, 9943, 16334, 68862, 9011, 14031, 6178, 21225, 1420, 32236, 2099, 2150, 26583, 2784, 8941, 9811, 27444, 50566 or 66428 molecules

	Issue Date	Pages	Document ID	Title
19	20030703	47	US 20030125533 A1	Regulation of human sphingosine kinase-like protein
20	20030522	61	US 20030096022 A1	Compositions and methods for the treatment and prevention of cardiovascular diseases and disorders, and for identifying agents therapeutic therefor
21	20030206	60	US 20030027304 A1	Compositions and methods for the treatment and prevention of cardiovascular diseases and disorders, and for identifying agents therapeutic therefor
22	20030206	60	US 20030026799 A1	Compositions and methods for the treatment and prevention of cardiovascular diseases and disorders, and for identifying agents therapeutic therefor
23	20021226	34	US 20020197654 A1	Method for measuring serine palmitoyltransferase in mammalian tissue and use thereof
24	20020725	26	US 20020099029 A1	Induction of blood vessel formation through administration of polynucleotides encoding sphingosine kinases
25	20020411	24	US 20020042358 A1	Sphingosine kinase, cloning, expression and methods of use
26	20020411	41	US 20020042101 A1	Mammalian sphingosine kinase type 2 isoforms, cloning, expression and methods of use thereof

	Issue Date	Pages	Document ID	Title
27	20020411	19	US 20020042091 A1	Methods and compositions for screening modulators of lipid kinases
28	20011115	32	US 20010041688 A1	Methods and compositions for the regulation of vasoconstriction
29	20050419	64	US 6881546 B2	Compositions and methods for the treatment and prevention of cardiovascular diseases and disorders, and for identifying agents therapeutic therefor
30	20050222	66	US 6858383 B2	Compositions and methods for the treatment and prevention of cardiovascular diseases and disorders, and for identifying agents therapeutic therefor
31	20041214	22	US 6830916 B2	Sphingosine kinase, cloning, expression and methods of use
32	20041214	46	US 6830881 B2	Sphingosine-1-phosphate lyase polypeptides, polynucleotides and modulating agents and methods of use therefor
33	20041005	41	US 6800470 B2	Mammalian sphingosine kinase type 2 isoforms, cloning, expression and methods of use thereof
34	20040504	60	US 6730480 B1	Sphingosine kinase enzyme
35	20040420	19	US 6723525 B2	Methods and compositions for screening modulators of lipid kinases
36	20030826	25	US 6610534 B2	Induction of blood vessel formation through administration of polynucleotides encoding sphingosine kinases

	Issue Date	Pages	Document ID	Title
37	20021119	59	US 6482609 B1	Isolated human EDG-4 receptor and polynucletide encoding said receptor

	Issue Date	Pages	Document ID	Title
1	20050609	56	US 20050123942 A1	Novel sphingosine kinases
2	20050512	39	US 20050100547 A1	Sphingosine kinase interacts with traf2 and modulates tumor necrosis factor-induced cellular activity
3	20050407	24	US 20050074830 A1	Screening method for an agent having an affect on a sphingosine kinase signaling pathway
4	20050113	35	US 20050009732 A1	Method of treatment and agents useful for same
5	20041209	54	US 20040247603 A1	Compositions and methods for the treatment and prevention of cancer, angiogenesis, and inflammation
6	20041028	34	US 20040214319 A1	Methods of regulating differentiation in stem cells
7	20041014	42	US 20040203104 A1	Mammalian sphingosine kinase type 2 isoforms, cloning, expression and methods of use thereof
8	20040902	94	US 20040171037 A1	Amplified genes involved in cancer
9	20040715	17	US 20040137447 A1	Human sphingosine-1-phosphate phosphatase
10	20040708	58	US 20040132053 A1	Sphingosine kinase enzyme
11	20040422	151	US 20040077044 A1	Kinases and phosphatases
12	20040226	152	US 20040038881 A1	Human kinases
13	20040122	20	US 20040014635 A1	Sphingosine kinase and uses thereof

	Issue Date	Pages	Document ID	Title
14	20040108	345	US 20040005563 A1	Methods of diagnosis of ovarian cancer, compositions and methods of screening for modulators of ovarian cancer
15	20031106	148	US 20030207299 A1	Human kinases
16	20030821	80	US 20030157082 A1	Methods and compositions for treating cancer using 140, 1470, 1686, 2089, 2427, 3702, 5891, 6428, 7181, 7660, 25641, 69583, 49863, 8897, 1682, 17667, 9235, 3703, 14171, 10359, 1660, 1450, 18894, 2088, 32427, 2160, 9252, 9389, 1642, 85269, 10297, 1584, 9525, 14124, 4469, 8990, 2100, 9288, 64698, 10480,20893, 33230,1586, 9943, 16334, 68862, 9011, 14031, 6178, 21225, 1420, 32236, 2099, 2150, 26583, 2784, 8941, 9811, 27444, 50566 or 66428 molecules
17	20030522	61	US 20030096022 A1	Compositions and methods for the treatment and prevention of cardiovascular diseases and disorders, and for identifying agents therapeutic therefor

	Issue Date	Pages	Document ID	Title
18	20030206	60	US 20030027304 A1	Compositions and methods for the treatment and prevention of cardiovascular diseases and disorders, and for identifying agents therapeutic therefor
19	20030206	60	US 20030026799 A1	Compositions and methods for the treatment and prevention of cardiovascular diseases and disorders, and for identifying agents therapeutic therefor
20	20020627	57	US 20020082203 A1	Novel sphingosine kinases
21	20020502	25	US 20020051777 A1	Method of modulating cellular activity
22	20020411	41	US 20020042101 A1	Mammalian sphingosine kinase type 2 isoforms, cloning, expression and methods of use thereof
23	20020131	24	US 20020012984 A1	Mammalian sphingosine - 1 - phosphate phosphatase
24	20050419	64	US 6881546 B2	Compositions and methods for the treatment and prevention of cardiovascular diseases and disorders, and for identifying agents therapeutic therefor
25	20050222	53	US 6858427 B2	Sphingosine kinases
26	20050222	66	US 6858383 B2	Compositions and methods for the treatment and prevention of cardiovascular diseases and disorders, and for identifying agents therapeutic therefor

	Issue Date	Pages	Document ID	Title
27	20041005	41	US 6800470 B2	Mammalian sphingosine kinase type 2 isoforms, cloning, expression and methods of use thereof
28	20040504	60	US 6730480 B1	Sphingosine kinase enzyme
29	20031223	23	US 6667163 B2	Polynucleotide sequences encoding mouse sphingosine-1-phosphate phosphatase
30	20031118	23	US 6649362 B2	Screening method for an agent having an effect on a sphingosine kinase signaling pathway